

ORIGINAL ARTICLE

Correlation of Stroke Risk Factor With Outcome in Non-thrombolysis Acute Ischemic Stroke Patients

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ABSTRACT

Introduction: Stroke is the second leading cause of death and the third leading cause of chronic disability worldwide with over 50% of survivors. Indonesia has the highest stroke mortality rate among countries in Asia. Stroke is associated with modifiable and non-modifiable risk factors. Stroke patients will have limitations in their daily activities. The limitations vary depending on their outcomes. This study aims to determine the correlation between stroke risk factors and stroke outcomes. **Materials and methods:** This research used cross-sectional observational analytic study and non-probability sampling with total sampling technique. The research subjects consisted of 77 non-thrombolysis acute ischemic stroke patients who came to the emergency room of Mohammad Noer General Hospital from September 2022 to February 2023. The stroke risk factors were assessed using the R-FSRS (Revised Framingham Stroke Risk Score) and patient outcomes were assessed using the NIHSS (National Institutes of Health Stroke Scale). **Results:** The correlation between the risk factor of stroke were assessed using the R-FSRS and the outcome of non-thrombolysis acute ischemic stroke patients was significant with a P value <0.001. The correlation between blood pressure and type 2 diabetes mellitus with stroke outcome as assessed by the NIHSS was significant with a P value <0.001. **Conclusion:** There was significant correlation between the risk factor of stroke as assessed by R-FSRS and the outcome of stroke as assessed by NIHSS in ischemic stroke patients. Hypertension and diabetes mellitus are the predominant risk factors of stroke.

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INTRODUCTION

The World Health Organization defined stroke clinically as a sudden focal or generalized neurologic deficit of more than 24 hours or leading to death caused by vascular disorders in the brain (1). Stroke is the second leading cause of death worldwide with a mortality rate of approximately 5 million people annually. Stroke is also the third leading cause of disability with over 50% of survivors being chronic disability (2,3). There were 25.7 million stroke patients in the world with 6.5 million deaths and 11.3 million having disabilities. In the last 2 decades, the stroke incidence had increased to 70.0%, the mortality rate had increased to 43.0%, the prevalence had increased to 102.0%, and the DALYs (disability-adjusted life years) of stroke had increased to 143.0%. The increase in stroke-related DALYs occurred

in low and middle income countries, while in high income countries, there was a decrease (4).

Stroke was the number one cause of death in Indonesia with mortality rate of around 300 thousand people (21% of all deaths) (5). Indonesia has the highest stroke mortality rate among countries in Asia with a mortality rate of 193 per 100,000 population per year (6). Stroke is still the most common non-communicable diseases in Indonesia. In 2013 and 2018, the prevalence of non-communicable diseases was an increase, especially cardiovascular diseases. These non-communicable diseases are associated with modifiable and non-modifiable risk factors (7).

Stroke is a disease related to lifestyle, over 90% of stroke risk factors worldwide are caused by modifiable risk factors (8). Nearly 90% of all strokes can be prevented with lifestyle modifications (9). Primary prevention of stroke is very important because 77% of strokes occur for the first attack. In people with a healthy lifestyle, the risk of the first stroke event is reduced by up to 80%

(10). But in Indonesia, stroke prevention programs are still lacking (11).

Stroke causes long-term disability with more than 40% of survivors depending on others for their daily activities. Stroke incidence in patients will affect the lives of patients and their families (12). A stroke patient's limitations vary depending on the stroke outcome. Therefore, the outcome of stroke needs to be assessed for further treatment and patient prognosis in the future (1). This research was designed to evaluate the correlation of stroke risk factors with non-thrombolytic acute ischemic stroke patients' outcomes.

MATERIALS AND METHODS

Study Design

This research used a cross-sectional observational analytic study and non-probability sampling with a total sampling technique.

Study Location and Population

The research subjects consisted of 77 non-thrombolysis acute ischemic stroke patients who came to the emergency room of Mohammad Noer General Hospital, Indonesia from September 2022 to February 2023. The inclusion criteria in this research study were ischemic stroke patients, the first attack of stroke patients, acute onset of stroke in less than 24 hours, and non-thrombolysis patients. The exclusion criteria in this study were hemorrhagic stroke patients, the second attack of stroke patients, onset of stroke more than 24 hours, thrombolysis patients, and sepsis patients.

Data Collection and Analysis

At the time of collecting the data, the researcher will immediately examine the patient who comes to the emergency room. The risk factors of stroke were assessed using the Revised-Framingham Stroke Risk Score (R-FSRS). Calculation of R-FSRS using the formula in the study of Dufouil et al., 2017 (Fig. 1). Stroke patient outcome was assessed using the National Institutes of Health Stroke Scale (NIHSS). The interpretation is mild in patients with scores 1-4, moderate in patients with scores 5-15, severe in patients with scores 16-20, and very severe in patients with scores 21-42 (17). IBM SPSS Statistics 25 was used for data analysis in this study. Analysis data of correlation of stroke risk factor with non-thrombolysis acute ischemic stroke patients' outcome using spearman's correlation. Mann-Whitney U test was used to determine the correlation between sex, diabetes mellitus, and smoking with the outcome of stroke. Kruskal-Williss test was used to determine the correlation between age and blood pressure and the outcome of stroke.

Ethical Clearance

This study was approved by the Ethics Committee of Slamet Martodirjdo General Hospital, Pamekasan,

Indonesia. The number of ethical clearances is No.070/083/432.603/KEPK/2022. This study was also approved by Mohammad Noer General Hospital for research in that hospital.

RESULTS

The research subjects in this study totaled 77 patients with 36 men (46.8%) and 41 women (53.2%). The youngest age is 34 years and the oldest is 90 years with a median age of 57 years. There were 20 patients (25.9%) aged ≤49 years, 25 patients (32.5%) aged 50-59 years, 23 patients (29.8%) aged 60-69 years, and 9 persons (11.7%) aged ≥70 years. The education of research subjects is 7 patients (9.1%) unschooled, 36 patients (46.8%) elementary school, 9 patients (11.7%) middle school, 19 patients (24.7%) high school, and 6 patients (7.8%) diploma/bachelor degree. This research was dominated by Madurese with 73 patients (94.8%) because this study was conducted at the Mohammad Noer General Hospital, which is located on Madura Island. Most of the research subjects worked as housewives and farmers with a total of 24 patients (31.2%) each, then 11 patients were unemployed (14.3%), 10 patients were self-employed (13.0%), 5 patients were civil servants (6.5%), fisher, driver, and security guard each 1 patient (1.3%). Most of the research subjects had hypertension with a total of 69 patients (89.6%), type 2 diabetes mellitus totaled 25 patients (32.5%), and cardiac disease amounted to 1 patient (1.3%). In this study, 32 research subjects had a history of smoking risk factors and all of them were male (Table I).

Table I: Characteristics of the Research Subjects

Characteristic	Frequency (%)	Median (min-max)
Age		
≤49 years	20 (25.9)	57 (34-90)
50-59 years	25 (32.5)	
60-69 years	23 (29.8)	
≥70 years	9 (11.7)	
Sex		
Male	36 (46.8)	
Female	41 (53.2)	
Education		
Unschooled	7 (9.1)	
Elementary school	36 (46.8)	
Middle school	9 (11.7)	
High school	19 (24.7)	
Diploma/Bachelor degree	6 (7.8)	
Race		
Madurese	73 (94.8)	
Javanese	4 (5.2)	
Profession		
Housewife	24 (31.2)	
Farmer	24 (31.2)	
Unemployed	11 (14.3)	
Self-employed	10 (13.0)	
Civil servant	5 (6.5)	
Fisher	1 (1.3)	
Driver	1 (1.3)	
Security guard	1 (1.3)	

CONTINUE

Table I: Characteristics of the Research Subjects (CONT.)

Characteristic	Frequency (%)	Median (min-max)
History of disease		
Hypertension	69 (89.6)	
Diabetes Mellitus type 2	25 (32.5)	
Cardiac Disease	1 (1.3)	
Atrial Fibrillation	0 (0)	
Risk Factor		
Smoking History	32 (41.6)	
Alcohol History	0 (0)	

Table II: Correlation between R-FSRS and NIHSS

Categorization of NIHSS	Frequency (%)	Median of R-FSRS (min-max)	P
Mild	23 (29.9)	1.48% (0.15% - 14.12%)	<0.001
Moderate	32 (41.6)	5.66% (0.26% - 36.80%)	
Severe	13 (16.9)	16.80% (3.01% - 42.98%)	
Very Severe	9 (11.7)	9.82% (0.14% - 54.40%)	

Based on the results of this research, there were 23 stroke patients (29.9%) who had mild outcomes with a median R-FSRS of 1.48% and a range between 0.15% - 14.12%. Most of the research subjects were in the moderate outcome category with a total of 32 patients (41.6%) with a median R-FSRS of 5.66% and a range between 0.26% - 36.80%. A total of 13 patients (16.9%) had a severe stroke with a median risk of 16.80% and a range of 3.01% - 42.98%. A total of 9 patients (11.7%) had a very severe stroke and all patients in this category were in a coma. The median in this category was 9.82% with a range of 0.14% - 54.40%. This study also found a significant correlation with a P value <0.001 between the

Table III: Correlation of Stroke Risk Factor with NIHSS

Stroke Risk Factor	R-FSRS Median (Min-Max)	NIHSS (n)				P
		Mild	Moderate	Severe	Very Severe	
Age						
≤49 years	1.51% (0.14%-35.11%)	8	7	2	2	0.116
50-59 years	4.05% (0.63%-22.05%)	8	8	4	6	
60-69 years	8.60% (1.37%-54.40%)	3	7	9	3	
≥70 years	16.47% (5.63%-42.98%)	1	3	3	3	
Sex						
Male	9.97% (1.37%-54.40%)	12	13	8	3	0.734
Female	1.58% (0.14%-42.98%)	11	19	5	6	
Blood Pressure						
Normal	2.89% (0.15%-5.63%)	1	0	0	1	<0.001
Pre-Hypertension	1.09% (0.35%-6.15%)	6	0	0	0	
Hypertension Grade 1	3.11% (0.63%-17.02%)	10	5	2	0	
Hypertension Grade 2	7.37% (0.14%-54.40%)	5	14	6	3	
Diabetes Mellitus Type 2						
Yes	9.82% (0.35%-54.40%)	2	8	7	8	<0.001
No	3.57 (0.14%-42.98%)	21	24	6	1	
Smoker						
Yes	11.13% (2.24%-54.40%)	9	12	8	3	0.592
No	1.7% (0.14%-42.98%)	14	20	5	6	

risk factor of stroke assessed by R-FSRS and the outcome of stroke assessed by NIHSS (Table II).

In this study, the correlation between blood pressure and type 2 diabetes mellitus with stroke outcome as assessed by the NIHSS was significant with a P value <0.001. Meanwhile, for age, sex, and smoking, there was no significant correlation with stroke outcomes with P values of 0.116, 0.734, and 0.592. At normal blood pressure, there was 1 patient each with mild and very severe stroke outcomes. At pre-hypertension blood pressure, there were 6 patients with mild stroke outcomes. In hypertension grade 1, most stroke patients' outcome was mild (10 patients). In hypertension grade 2, most stroke patients' outcome was moderate (14 patients). In type 2 diabetes mellitus patients, the majority of stroke outcome was very severe and moderate with a total of 8 patients each. However, in non-diabetes mellitus, the majority of stroke outcome was moderate with total of 24 patients. In the age category, the majority of stroke outcome in patients aged ≤49 years was mild with total of 8 patients. The majority of stroke outcome in patients aged 50-59 years was mild and moderate with total of 8 patients each. In patients aged 60-69 years, most stroke patients' outcome was severe (9 patients). In patients aged ≥70 years, most stroke patients' outcome was moderate, severe, and very severe with 3 patients each. In the sex category, the most outcome of stroke in male patients was moderate with total of 13 patients and in females, the most outcome was moderate with total of 19 patients. In this research, the most outcome of stroke in smoker patients was moderate with total of 12 patients and the most outcome of stroke in non-smoker patients was moderate outcome with total of 20 patients (Table III).

$$FSRP(t) = 1 - Sb(t)^{\exp(L-M)}$$

For Woman, M=6.6170719, Sb(10)=0.95911

$$FSRP(10) = 1 - (0.95911)^{\exp(L-6.6170719)}$$

With L = 0.87938 x (age/10) + 0.51127 [if smoker] - 0.03035 [if CVD] + 1.020720 [if AF] + 0.39796 [if age≥65] + 1.07111 [if age<65 and DM] + 0.06565 [if age ≥65 and DM] + 0.13085 [if on antihypertensive medication] + 0.11303 x (SBP-120)/10 [if no antihypertensive medication] + 0.17234 x (SBP-120)/10 [if on antihypertensive medication]

For Man, M=4.4227101, Sb(10)=0.94451

$$FSRP(10) = 1 - (0.94451)^{\exp(L-4.4227101)}$$

With L = 0.49716 x (age/10) + 0.47254 [if smoker] + 0.45341 [if CVD] + 0.08064 [if AF] + 0.45426 [if age≥65] + 1.35304 [if age<65 and DM] + 0.34385 [if age ≥65 and DM] + 0.82598 [if on antihypertensive medication] + 0.27323 x (SBP-120)/10 [if no antihypertensive medication] + 0.09793 x (SBP-120)/10 [if on antihypertensive medication]

Figure 1: Formula of R-FSRS.

DISCUSSION

Clinical tools for predicting disease are important for further management and are used for individuals to modify lifestyles that can reduce risk factors. There are several risk scores for predicting stroke. The FSRS is the most well-known and well-accepted risk score worldwide. This risk score was developed in the 1990s during a period of higher stroke risk. The FSRS factor consists of age, sex/gender, systolic blood pressure, diabetes mellitus, use of antihypertensive drugs or not, the prevalence of cardiac disease, atrial fibrillation, smoking, and left ventricular hypertrophy (13). However, in 2018 there was a revision of the FSRS. The calibration for incident stroke in the R-FSRS score is better than the O-FSRS score. In R-FSRS there is no left ventricular hypertrophy factor. The R-FSRS was developed to reflect the updated stroke risk prevalence and may be used for multiple geographic or racial differences worldwide (14).

Several stroke deficit scales had been used before. The NIHSS is the most commonly used deficit scale for assessing the severity outcome of stroke worldwide. Originally, the NIHSS was used as a study instrument for measuring baseline data in clinical trials of acute stroke patients. Since 1995, the NIHSS has been the standard for assessing clinical deficits in stroke patients (15,16).

In this research study, a significant correlation was obtained between the risk factor for stroke assessed by R-FSRS and the outcome of stroke assessed by NIHSS. The higher value of R-FSRS, the more severe the stroke outcome in ischemic stroke patients. The study by Soliman et.al, 2018 shows the correlation between risk factors of stroke with the severity of stroke was obtained. The most prevalent risk factors are hypertension and older patients. That’s probably due to the severity of stroke patients (10). The research by Vahdari et.al. 2018 also shows the correlation between stroke risk factors with the severity of stroke patients, especially hypertension, older age, positive family history, and atrial fibrillation (AF) are significant (17). In a research study by Mulugeta et.al 2020, the correlation between stroke risk factors

and poorer outcomes was significant in stroke patients, especially hypertension, hyperlipidemia, sex, and atrial fibrillation (18). All major risk factors can be assessed through the R-FSRS where each component is assessed. Hypertension and diabetes mellitus are the predominant risk factors of stroke. Hypertension is the strongest and most prevalent stroke risk factor worldwide. In hypertension patients, there is initiation and acceleration of intracerebral vasculopathy and also the development of the atherosclerotic disease that can lead to stroke (19–21). In this research, the correlation between blood pressure levels and stroke outcomes was significant. The group with high blood pressure will have more severe outcomes than the group with lower blood pressure. Our results study is in line with the research study by Malhotra et al 2020, increased blood pressure levels were associated with poor clinical outcomes of stroke (22). Diabetes mellitus is a modifiable stroke risk factor, especially ischemic stroke. In diabetics, systemic inflammation, arterial stiffness, and endothelial dysfunction can lead to stroke. In diabetes mellitus patients, the risk of stroke and mortality increases compared to non-diabetes mellitus. Hyperglycemia during acute stroke is related to poor outcomes (23,24). In this research study, the correlation between diabetes mellitus and the severity of stroke outcomes was significant. Diabetes mellitus patients had poorer outcomes than non-diabetic patients. Our results study is in line with the meta-analysis study by Lau et al 2019, diabetes mellitus is correlated with adverse outcomes of stroke compared to non-diabetes mellitus (25). In the meta-analysis study by Mosenzon et al 2023, diabetes mellitus was correlated with worse stroke outcomes. Patients with diabetes mellitus had adverse stroke outcomes and a higher risk of stroke recurrence compared with non-diabetes mellitus patients (26).

This research is the first research study that investigates the correlation between the risk factor for stroke assessed by R-FSRS and the outcome of stroke assessed by NIHSS in ischemic stroke patients. However, this research has limitations, that is limited research subjects and this research used a cross-sectional study method. This limitation occurs because the researcher has limited time and place for research. Further research is needed with more research subjects and better use of the cohort study method.

CONCLUSION

There was a significant correlation between stroke risk factors as assessed by R-FSRS and the outcome of stroke as assessed by NIHSS in non-thrombolysis acute ischemic stroke patients. The higher the R-FSRS value, the more serious the stroke outcome in ischemic stroke patients. Hypertension and diabetes mellitus are the predominant risk factors of stroke. These findings can be used for further research and can be used for primary health care for predict the stroke and outcome of stroke

by R-FSRS.

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