Framingham Risk Score (FRS) as Risk Factor of Stroke

Saugi Abduh[a], Indah Wardani[b], Siti Thomas Zulaikhah[c*]

[a]Departement of Intenal Medicine, Faculty of Medicine, Universitas Islam Sultan Agung, Jln. Raya Kaligawe
KM. 4 Semarang, 50112

[b]Student of Faculty of Medicine, Universitas Islam Sultan Agung, Jln. Raya Kaligawe KM. 4 Semarang, 50112

[c]Departement of Public Health, Faculty of Medicine, Universitas Islam Sultan Agung, Jln. Raya Kaligawe KM.
4 Semarang, 50112

[a]Email: drsaugiabduh@yahoo.com

[b]Email: wardaniindah@yahoo.com

[c]Email: sitithomas@unissula.ac.id

Abstract

Stroke is the leading cause of death and disability in many parts of the world, including Indonesia. Stroke
incidence has been increasing. A number of stroke risk factors have been identified, Framingham Risk Score
(FRS) can be used as a predictor of stroke. This study aimed to determine the relationship between FRS and
stroke. **Methods**: This was a cross-sectional study among 70 consecutive in-patients at Sultan Agung Islamic
Hospital, Semarang, Indonesia. The data were obtained from medical records were analyzed using Chi Square
for bivariate test and multiple logistic regression for multivariate test. The result of bivariate analysis showed a
significant relationship between total FRS and stroke with p = 0.018 (<0.05), while components of FRS
correlated to stroke were age (p = 0.034), diabetes mellitus (DM) (p = 0.046), hypertension (p = 0.037),
hypertension treatment (p = 0.015) and smoking (p = 0.031). The results of multivariate analysis for each
component showed that the most dominant FRS associated with stroke was DM (PR = 8.522; 95% CI = 1.736 -
41.846). There was a relationship between total FRS and stroke. Risk factors of FRS components associated
with stroke were age, hypertension, DM, hypertension and smoking. DM was the most dominant risk factor
associated with stroke, patients with DM has 8.522 times higher risk of developing stroke compared to those
without.

Keywords: Stroke; Framingham Risk Score; Diabetes mellitus.

----

* Corresponding author.

1. Introduction

Stroke is an acute nerve function disorder due to circulatory disorders to the brain. Its symptoms depend on which area of focal region of the brain is affected [1]. Stroke is the fifth leading cause of death in the United States killing nearly 130,000 people every year accounting for one in 20 deaths. In United State, every 40 seconds, someone has a stroke and every four minutes, 2 people die from stroke. Every year about 795,000 people in the United States have a stroke. A total of 610,000 of these are the new strokes and 185,000 are recurrent strokes [2]. According to the American Heart Association National Center in 2015, the oldest stroke patients in 2009 to 2012 was above 80 years accounting for 29.8%. Based on gender, prevalence of stoke in male and female was 24% and 23%, respectively [3].

The prevalence of stroke, heart failure and coronary heart disease in Indonesia based on the Indonesian Basic Health Research (*Riskesdas*) in 2013 was 12.1%, 0.3%, 1.5% respectively meaning that stroke ranked first in the most leading fatal non-infectious. The prevalence of stroke increases with age ($\geq$ 75 years 43.1% and 67.0%) [4]. The prevalence of store in men are similar to that of women [5].

There are numbers of risk factors of stroke including biological conditions such as age and sex, other factors such as high blood pressure, serum cholesterol, fibrinogen, smoking behaviors, diet, alcohol consumption, lack of physical activity, non-hemorrhagic heart disease, atrial fibrillation, glucose intolerance, social characteristics such as education, social class, ethnicity and physical environmental factors (temperature, geography and psychology) [6].

A research conducted in Malaysia involving 14,863 respondents aged 40-65 years comparing Framingham Risk Score (FRS), systematic coronary risk evaluation (SCORE) and the World Health Organization (WHO) / International Society of Hypertension(ISH) for measuring the risk factor for cardiovascular disease in the Asian population recommended FRS and SCORE for practitioners in Malaysia despite the difference in use of the two models.

For male patients SCORE was recommended while for women FRS was recommended [7].

Measurement of risk factors suing FRS can be performed with an online calculator that includes various indicators [7]. FRS can predict the development of stroke based on the calculation of risk factors including age, systolic blood pressure, antihypertensive drugs, diabetes, smoking status, history of cardiovascular disease, atrial fibrillation, and left ventricular hypertrophy [8].

The FRS results are used to predict coronary heart disease, myocardial infarction, coronary insufficiency, angina, non-hemorrhagic stroke, hemorrhagic stroke, transient ischemic attack, peripheral artery disease, heart failure within the for the following 10 years. Use of FRS is recommended for subjects <85 year [9].

The Prevalence of stroke in Indonesia is high. This study aimed to identify the risk factors that contribute to the development of stroke using FRS to determine its relationship to non-hemorrhagic stroke and hemorrhagic stroke at Sultan Agung Islamic Hospital Semarang, Indonesia.

2. Methods

This was a cross sectional study. The independent variables   included   age, sex, systolic blood pressure, antihypertensive drug use, diabetes mellitus , smoking according the   criteria   of Adult Treatment Panel III criteria , an expert panel of   National Heart,   Lung, and Blood Institute which is part of National Institutes of Health   (NIH) USA. Data were categorized into three: low risk (<10%), medium risk (10-20%), and high risk (> 20%). The dependent variables were stroke patients being hospitalized and had been diagnosed with non-hemorrhagic or haemorrhagic stroke by a doctor in a neurology ward with CT-Scan or MRI. The population was of all stroke patients undergoing hospitalization at Sultan Agung Semarang Islamic Hospital between January 1, 2015 and December 31, 2016.

Seventy consecutive patients were included from the medical records of the hospital.

The sample was a part of the population meeting the inclusion criteria of 55-85 years old, complete medical record including the information of patient register number, age, sex, ECG examination, systolic blood test result, smoking history, diabetes mellitus, history of treatment of hypertension, history of heart disease, atrial fibrillation and left ventricular hypertrophy.

The exclusion criteria were patients diagnosed with obstructive sleep apnea syndrome, having a history of Transient Ischemic Attacks (TIA), blood disorders such as sickle-cell disease, a history of stroke in family members and have blood viscosity disorders such as polycythemia.

3. Result

The result of bivariate analysis with chi-square test between level FRS and stroke resulted in p value of 0.018 (<0.05) meaning that there was a relationship between the level FRS and stroke (table 1).

The results of p value on each FRS variables were age (0.034), hypertension (0.449) , smoking habit (p = 0.031) and hypertension (0.037), use of antihypertensive drugs (0.015), diabetes mellitus (0.046), history of heart disease (0.181), left ventricular hypertrophy (0.846) and atrial fibrillation (0.524) (table 2). This variables in FRS positively associated with stroke were age, smoking, hypertension, antihypertensive medication use, diabetes mellitus (DM). Variables that can be analyzed with multivariate analysis was variable which in result of bivariate analysis have value p > 0,25.

Results of the multivariate analysis is   presented   in Table 3 showing that the analysis of the variables of age, smoking, hypertension, use of antihypertensive drugs, diabetes mellitus (DM), and a history of heart disease showed that DM and smoking habits were significantly associated with stroke.

DM is the most dominant risk factor associated with stroke, where patients with DM had 8.522 times higher risk for stroke compared with those without (PR = 8.522; 95% CI = 1.736 - 41.846). Likewise, smokers had 5.935 times higher risk to get stroke compared with nonsmokers (PR = 5.935; 95% CI = 1,439 - 24,442).

Table 1: Relationship between Framingham Risk Score and Stroke

Bivariate Analysis		Stroke				number		p value
		Hemorrhagic		Non-Hemorrhagic				
		n	(%)	n	(%)	n	(%)	
Framingham Risk Score	High	9	56.3	7	43.8	16	100	0.018
	Medium	3	15.8	16	84.2	19	100	
	Low	8	22.9	27	77.1	35	100	
Totality		20	28.6	60	71.4	70	100	

Table 2: Analysis of Risk Factors relating to Stroke

Factor	p value
Age	0.034 *
Gender	0.449
Smoking habit	0.031 *
Hypertension	0.037 *
Use of Antihypertensive Drugs	0.015 *
Diabetes mellitus (DM)	0.046 *
Heart Disease History	0.181
Left Ventricular Hypertrophy	0.846
Atrial Fibrillation	0.524

* = significant (<0.05)

Table 3: Results of Multivariate Analysis

Variables	p value	PR	95% CI
Age	0.028	0.270	0.084-0.866
Smoking habit	0.014	5.935	1.479-24.442 *
Hypertension	0.077	0.536	0.268-1.070
Use of Antihypertensive Drugs	0.264	2.234	0.545-9.148
Diabetes mellitus (DM)	0.008	8.522	1.736-41.846 *
Heart Disease History	0.440	1.762	0.418-7.422

4. Discussion

The results of this study indicate that there was a correlation between FRS level and stroke; the components in FRS significantly associated with stroke were age, smoking habit, hypertension, antihypertensive drug use, diabetes mellitus (DM). The study by Arboix (2008) among 218 men and 127 women in Spain reported that 93% of stroke patients were older than 64 years [10]. Sacco Research (2016) reported that age was the most important risk factor in stroke. According to the ASNA Survey (ASEAN Neurological Association) stroke patients were under 45 years (11.8%), 45-64 years (54.2%) and over 65 years (33.5%). Meanwhile, based on the addition of points Framingham Risk Score, with age, the higher score is given. This means that the higher the Framingham Risk Score, the higher the risk of stroke a patient has. The frequency of stroke increases with age due to decline in bodily function especially the blood vessels of the brain. The blood vessels become less elastic leading to a higher risk of endothelium thickening. Such thickening often occurs in the intima so that blood flow decreases and causes a blockage in the blood vessels of the brain [11].

Hypertension is a risk factor associated with stroke. This finding is in accordance with research Geyer (2009) who reported that hypertension has a strong correlation in stroke [12]. Any increase in blood pressure, the higher the risk factor for stroke. It becomes very powerful at all if blood pressure reaches 160/95 mmHg. Study Nuraini show that several factors are known to cause hypertension consist of causal that can be modified (diet, obesity, smoking, diabetes and diseases) and the causes that can not be modified (age, ras, sex and genetics)[13]. In the measurement of FRS showed an increased risk of cerebral infarction in hypertensive patients. Hypertension increases the risk of stroke types such as thrombosis, lacunar stroke, hemorrhagic stroke and hemorrhagic subarachnoid stroke. On the addition of Framingham Risk Score the higher the systolic data the higher the point. This means that the higher the number on the FRS the higher the risk of stroke. Hypertension accelerates the occurrence of atherosclerosis (buildup of cholesterol in the artery walls) by causing mechanical injury to endothelial cells where high pressure will stimulate the formation of atherosclerotic plaques in the arteries and arterioles (small branches of the arteries) in the brain and induce lipohyalinosis (vascular damage characterized by loss of normal arterial structures, foam cells and the presence of fibrinoid neck wall vessels) in the basal ganglia vessels, leading to lacunal infarction or cerebral hemorrhage [14].

During the years of monitoring of the framingham study population, the Framingham Heart Risk Score (FHRS) has resulted in the identification of risk factors for cardiovascular disease. Framingham Stroke Risk Score (FSRS) for the most famous stroke risk score developed during the period when the prevalence of high stroke risk was from 1990 [15]. FRS is a common predictor for the risk of atherotrombotic disease. Based on the Framingham Score Study, the output of the Framingham Risk Score assessment includes cardiovascular disease (coronary heart, myocardial infarction, coronary insufficiency and angina). FRS is also used for predicting cerebrovascular disease, non-hemorrhagic stroke, hemorrhagic stroke and transient ischemic attack and peripheral artery disease [16].

This study shows that DM is the most dominant risk factor associated with stroke, where patients with DM 8.522 times are at risk of stroke compared with patients who are not DM (PR = 8.522; 95% CI = 1.736 - 41.846). These results are consistent with Sacco's (2016) study reporting that diabetes mellitus increases the

susceptibility of atherosclerosis and increases the prevalence of atherogenic risk factors, especially hypertension, obesity, and abnormal blood lipids [17]. A case-control study of stroke patients and prospective epidemiological studies has confirmed the independent effects of diabetes with a relative risk of non-hemorrhagic stroke in people with diabetes from 1.8 to 3.0. A study among Japanese patients in the Honolulu Heart Program, people with diabetes had two times higher risk of thromboembolism than people without diabetes. In a population-based cohort study in Rancho Bernardo, people with diabetes had a relative risk of stroke of 1.8 in men and 2.2 in women. In FRS measurement people with glucose intolerance have twice the risk of brain infarction than non-diabetes. While the addition of FRS points the status of diabetes gives a large enough points (+2). Thus, the higher the number of FRS, the higher the risk of stroke a patient has. DM causes blood coagulation due to high blood glucose levels, making it easy to thrombus. The resulting thrombus will cause atherosclerosis in the blood vessels that can cause constriction of blood vessels that lead to the brain [18]. High blood sugar levels in the body pathologically play a role in increasing the concentration of glycoprotein, which is the originator or risk factor of some vascular disease. In addition, the changes in the production of protacycline and decreased plasminogen activity in the blood vessels may stimulate the occurrence of thrombus. Diabetes mellitus will accelerate the occurrence of small and large blood vessel atherosclerosis throughout the body including the brain, which is one of the target organs of diabetes mellitus. High blood glucose levels during stroke will increase the likelihood of widespread infarction area due to the formation of lactic acid due to anaerobic glucose metabolism leading to damages of brain tissue [19]. A study by Kissela (2007) among African American showed that people with diabetes were more likely to have hypertension, myocardial infarction, and high cholesterol than non-diabetic patients [20]. These factors are the trigger factors of stroke. Diabetes increases the risk of stroke in all age groups and racial / ethnic groups. The study estimates that 37-42% of all non-hemorrhagic strokes in both African American races are caused by the effects of diabetes itself.

The results of this study stated that smoking is associated with stroke. Smokers have 5.935 times higher a risk of stroke compared with non-smoke (PR = 5.935; 95% CI = 1.439 – 24.442). Smoking increases the risk of stroke almost twice, with a clear dose response relationship. In the Framingham study and the Nurses' Health Study cessation of smoking led to a rapid decline in the risk of a reduced stroke within 2 to 4 years. This risk reduction occurs across age ranges in heavy and moderate smokers [17]. According to FRS smoking status provides an additional value of +3 points leading to increase in risk of stroke.

The higher the number of FRS, the higher the risk of stroke. Cigarettes contain a variety of substances that can increase the risk of cerebrovascular disease. Inside cigarettes contain nicotine, carbon monoxide, and other substances that potentially cause damage to blood vessel walls.

Cigarettes cause the decrease in elasticity of blood vessels that may cause hardening of the arteries and increasing blood clotting factors due to high blood fibrinogen levels. Increased levels of fibrinogen can facilitate the thickening of blood vessels that become narrow and stiff [21]. The speculative hypothesis suggests that smoking habits increase proteolytic enzymes released by macrophages in the lungs, and accelerate the onset of atherosclerosis. Smoking habits also cause temporary increases in blood pressure associated with nicotine use [22].

5. Conclusion

There was a relationship between FRS and stroke. The factors of FRS associated with stroke were age, hypertension, diabetes mellitus, treatment of hypertension and smoking. Diabetes mellitus is the most dominant risk factor associated with stroke

References

[1]. WHO. Stroke, Cerebrovascular accident. 2016

[2]. National Center for Chronic Disease Prevention and Health Promotion. Stroke Fact Sheet. Centers for Disease Control and Prevention. 2016

[3]. Mozaffarian D. et al. Heart Disease and Stroke Statistics. The American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics, Volume VI(8), pp 1-23. 2015

[4]. Departemen Kesehatan RI (Depkes RI). Riset Kesehatan Dasar (Riskesdas) 2013. Jakarta: Badan Penelitian dan Pengembangan Kesehatan. 2013

[5]. Brett, C., Fernando, B. R. & Gustavo, S. Diagnosis and Management of Cerebral Venous Thrombosis. Diagnosis of Cerebral Venous Thrombosis, Volume IX (9), pp. 201-210. 2007

[6]. Truelsen, T., Begg, S. & Mathers, C. The global burden of cerebrovascular. Global Burden of Disease, 2(8).2006

[7]. Selvarajah, S. et al. Comparison of the Framingham Risk Score, SCORE and WHO/ISH cardiovascular risk prediction models in an Asian population. International Journal of Cardiology, Volume CXLVI (1), pp 211-218. 2014

[8]. Donald, M. & Lloyd, J. Cardiovascular Risk Prediction. Volume XII(6). 2010

[9]. Sabayan, B. et al. Framingham Stroke Risk Score and Cognitive Impairment for Predicting First-Time Stroke in the Oldest Old. American Heart Association, Volume XLIV (7), pp 1866-1871. 2013

[10]. Arboix, A. et al. Atrial fibrillation and stroke: clinical presentation of cardioembolic versus atherothrombotic infarction. National Center for Biotechnology Information, Volume I(3), pp. 33-34. 2010.

[11]. Kristiyawati, S.P., Irawaty, D., Hariyati, Rr.T.S. Faktor Risiko yang Berhubungan dengan Kejadian Stroke di RS Panti Wilasa Citarum Semarang", Jurnal Keperawatan dan Kebidanan (JIKK), 1 (1), 2009.

[12]. Geyer, J.D. & Gomez,. C.R. Stroke. United States of America: Wolters Kluwer Bussiness.2009.

[13]. Nuraini B. Risk Factors of Hypertension. Medical Journal of Lampung University. 5(5), pp.10-19.2015

[14]. Nabyl. Deteksi Dini Gejala dan Pengobatan Stroke : Solusi Hidup Sehat Bebas Stroke. Yogyakarta: Aulia. 2012

[15]. McClure, L. et al. Assessing the performance of the Framingham Stroke Risk Score in the reasons for geographic and racial differences in stroke cohort. Miami: Regard. Volume II, pp 134-178. 2016.

[16]. William , E. & Feeman, . J. BGS Graph Predicts Better Than the Framingham Risk Score. Journal of Clinical Lipidology, Volume IV(3), pp. 203. 2010

[17]. Sacco, R. L. et al. Public Health Burden of Stroke. American Heart Association, 5(3), pp 57-64.2016

[18].Caplan, M., Andrian, J., Goldszmidt, M. & Louis, R. Essentioal Stroke. Jakarta: EGC. 2009.

[19]. Tugasworo D. Prevensi Sekunder Stroke dalam Management of Post Stroke. Semarang : Badan Penerbit UNDIP. 2007.

[20]. Kisela, F. Diabetes, the Metabolic Syndrome, and Ischemic Stroke. American Diabetes Association, Volume 30(12), pp. 3131-3140. 2007

[21]. Marliana, Y.Gambaran Faktor Risiko pada Penderita Stroke Iskemik di RSUP H. Adam Malik Medan Tahun 2010. Skripsi Sarjana (Diterbitkan). Medan: Universitas Sumatera Utara. 2009

[22]. Kawachi, A., Reena, S. & John , C. Smoking and stroke: the more you smoke the more you stroke. Expert Rev Cardiovasc Ther , Volume VII (2) , pp. 917–932. 2010.