Conference Paper

Recurrent Stroke among Patients at Indonesia's National Brain Center Hospital: Contributing Factors

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Abstract

This study aims to determine the risk of recurrent stroke among patients at the Indonesian national brain center (Rumah Sakit Pusat Otak Nasional, or RSPON) who have suffered a first stroke. In this retrospective study, all the patients who were selected had had their first stroke in 2014. The Kaplan-Meier and multivariate Cox regression methods of data analysis were utilized. The results show that the average survival period after stroke recurrence is 38 months, with the median being 25 months. Age, hypertension, obesity, and irregular control are the variables that play a key role in the recurrence of strokes. Stroke patients who did not control their conditions regularly after the first attack had an 8.7 times higher risk of stroke recurrence. The incidence of recurrent stroke before 15 months was higher in those who were overweight or obese (HR = 1.96 and 3.38), and those who had developed pre-hypertension (HR = 2.26). Additionally, at observation after 15 months, levels of grade 1 and 2 hypertension in the cohort were higher (HR = 2.86 and 2.07). To reduce the risk of recurrent stroke, there is a need for stroke prevention via routine medical examinations at clinics and community stroke seminars to raise awareness of the risks. In addition, the establishment of a stroke community association in each region is recommended.

Keywords: hypertension, recurrent stroke, irregular control, survival analysis

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1. INTRODUCTION

Stroke is a health problem that needs special attention as it can attack anyone at any time, regardless of race, gender or age. It isa brain disease that results from nerve-function disorder, either locally or more generally, and is often sudden and progressive [4]. Indonesia has the highest proportion of stroke sufferers in Asia and is also ranked fourth in the world for stroke incidence (after India, China, and America). It was the

most common cause of mortality in Indonesia in 2014, with 21% of deaths resulting from the disease [6].

Patients can experience a number of complications after a first stroke, including recurrent stroke, dementia, and depression. The risk of death increases after every recurrent stroke. According to Supriyadi (2012), recurrent stroke patients are twice as likely to die from a subsequent attack than those who suffer a first stroke due to heart disease or high cholesterol. Prencipe (in Siswanto 2005) has found that the mortality rate for a first stroke is 18–37%, but rises to 62% for recurrent strokes. The same study suggests that 25% of those who recover from a first stroke will have another stroke within 5 years.

"Rumah Sakit Pusat Otak Nasinal" (RSPON) is a specialist center that treats diseasesassociated with the brain and the nervous system. Its 2014 annual report shows that stroke is the most common disease treated by the center (323 patients in 2014). Moreover, 16% of these patients experienced another stroke during the same year. This study aims to determine the factors that contribute to recurrent stroke at RSPON.

2. METHODS

This retrospective-cohort study used a survival-analysis technique that included multivariate Cox regression analysis. The data-collectionmethod involved observing the participantsover a two-year period post-stroke and noting important events that occurred. The secondary data was obtained from the patient's medical registration records at RSPON for 2014. The inclusion criteria were patients at RSPON who had been diagnosed with stroke, who had complete medical records (including laboratory results). Based on these criteria, 238 patients of 323 were selected for the study.

3. RESULTS AND DISCUSSION

Table 1 shows that 109 (45.8%) of the 238 patients suffered from stroke recurrence. The number of male patients, 149 (62.6%), was higher than the number of female patients. It was found that 44.3% of the males had another stroke during the follow-up period, while 48% of females suffered from recurrence. In the < 60 years age group, 38% experienced stroke recurrence. For the ≥ 60 years age group, the recurrence figure was higher, at 52.8%.

The percentage of patients who had heart disease was 28.6. We found that there was no significant difference between patients with heart disease and patients without

heart disease, where stroke recurrence was concerned. In addition, 46% of the patients in the study were suffering from diabetes mellitus. Interestingly, stroke recurrence occurred more frequently (52.29%) in the group of patients that did not have diabetes mellitus than in the group that did (40.31% recurrence). The percentage of patients having irregular control treatment was 56.3. Importantly, only 10.57% of patients having regular control treatment experienced stroke recurrence, while 67.16% of patients in the "irregular control" group experienced another stroke event. In the study population, hypercholesterolemia was found in 82.4% of the patients. Of these, 48.98% suffered another stroke during the follow-up period. Of the remaining patients, who had normal cholesterol levels, recurrent stroke was experienced in 30.95% of cases.

The percentage of patients with stage 2 hypertension (54.2%) was higher than the percentages of patients with normal blood pressure (22.3%), with a pre-hypertension classification (8.8%), or with stage 1 hypertension (14.7%). Of those with normal blood pressure, 41.51% experienced stroke recurrence, while the figures for the pre-hypertension, stage 1 hypertension, and stage 2 hypertension groups were 52.38%, 40%, and 48.06%, respectively.

The percentage of overweight patients was higher (49.2%) than the proportion of patients with a normal BMI (42.9%) or the proportion of patients classified as obese (8.0%). In the normal weight category, 45.09% of patients experienced another stroke event, while the figures for the overweight group and the obese group were 47.86% 36.84%, respectively.

The contributory factors for recurrent stroke were found to be irregular control, diabetes mellitus, age, hypertension and obesity. In addition, the effects of diabetes mellitus, hypertension, obesity and age on the recurrence of stroke were dependent on time.

Those in the "irregular control" category were found to be at greater risk of recurrent stroke. The probability of recurrent stroke in patients undergoing regular control treatment was 11%, whereas the probability was 68% for those receiving irregular treatment. This shows that levels of control make a difference to the likelihood of subsequent stroke in patients who have suffered a first stroke. Indeed, patients who do not undergo regular control procedures have an 8.71 times higher risk of recurrent stroke.

This finding is in line with research conducted by Siswanto (2005), in which it was found that the risk of recurrent stroke in patients receiving irregular treatment was 3.84 times higher than for patients undergoing regular control treatment. The results suggest that a stroke patient who wants to control the condition and is willing to

TABLE 1: Distribution figures for stroke patients at RSPON in 2014.

Variable	Total Respondents		Recurrent Stroke Event		Survival Time (months)	
	n	(%)	n	%	Mean	Median
Sex						
Male	149	62.6	66	44.3	38.4	24.7
Female	89	37.4	43	48.3	37.5	25.2
Age						
< 60	115	48.3	44	38.3	29.9	26.2
≥ 60	123	51.7	65	52.8	40.5	24.6
Stroke Type						
Ischemic	124	52.1	58	46.8	38.1	25.0
Hemorrhagic	114	47.9	51	44.7	37.8	25.2
Heart Disease						
Yes	68	28.6	78	45.9	39.6	24.7
No	170	71.4	31	45.6	33.4	25.3
Diabetes Mellitus						
Yes	109	45.8	57	52.3	40.8	24.7
No	129	54.2	52	40.3	32.1	26.5
Irregular control						
Yes	134	56.3	90	67.2	28.0	19.6
No	104	43.7	11	10.6	56.7	46.3
Duration of hospitalization						
< 7 day	90	37.8	44	48.8	36.3	23.9
7-14 day	101	42.4	43	42.6	35.6	26.2
≥ 15 day	47	19.7	22	46.8	44.5	26.5
Hypercholesterolemia						
No	42	17.6	13	30.9	38.3	23.1
Yes	196	82.4	96	48.9	37.4	25.0
Hypertension						
Normal	53	22.3	22	41.5	47.1	25.3
Pre-hypertension	21	8.8	11	52.4	26.9	23.9
Hypertension stage 1	35	14.7	14	40.0	38.2	24.3
Hypertension stage 2	129	54.2	62	48.1	37.9	26.5
Obesity						
Normal	102	42.9	46	45.1	43.9	28.8
Overweight	117	49.2	56	47.9	32.7	24.6
Obese	19	8.0	7	36.8	37.7	25.0

TABLE 2: Final Cox regression model for the factors associated with recurrent stroke.

Contributing variables	β	Sig	Exp(β)	95%CI
Irregular Control	2.165	0.000	8.71	4.49-16.87
Diabetes Mellitus	-0.050	0.873	0.95	0.51-1.76
Age 60+ yrs	0.031	0.058	1.03	0.99 -1.06
Hypertension (Ref. Normal)				
Pre-hypertension	0.840	0.021	2.32	1.14 – 4.71
Hypertension stage 1	-1.168	0.69	0.31	0.88 – 1.09
Hypertension stage 2	-0.473	0.334	0.62	0.24 – 1.63
Obesity (Ref. Normal)		0.120		
Overweight	0.746	0.367	2.11	0.42 – 10.66
Obese	1.288	0.110	3.62	0.75 – 17.58

take medication regularly will avoid recurrent stroke. Regular monitoring is designed to facilitate early detection of increased risk of stroke recurrence, and enables anti-recurrence treatment to commence immediately. Prompt diagnosis and early treatment are essential for maximum recovery from stroke and for the prevention of recurrent stroke. Such an approach is consistent with the objectives of pharmacological therapy for stroke, which are: (1) enabling open artery occlusion and the reperfusion of ischemic brain tissue, (2) limiting the occurrence of occlusion thromboembolism, (3) increasing the tolerance of cells (nerve cells are ischemic), (4) preventing dangerous reperfusion, (4) preventing/treating complications and (5) preventing recurrent stroke.

The risk of recurrent stroke in patients who have diabetes mellitus is lower than for those who do not have the condition. This result might be affected by the fact that the Random Plasma Glucose test was not used to detect the disease in this study; rather, GDNPP was taken as a marker of diabetes mellitus. Moreover, the question of whether or not the diabetes was being controlled was not taken into account. There are possibilities of bias, therefore, in this result. It is known that high blood sugar levels in the pathology can increase the concentration of glycoprotein in the body, which is a risk factor for vascular disease. In addition, changes to protasiklin production and to plasminogen and blood-vessel activity can stimulate the thrombus. Diabetes mellitus will accelerate small and large blood vessels throughout the body, including the brain, which is one of the target organs of diabetes mellitus. As such, a high blood glucose level will increase the likelihood of the spread of an infarcted area because lactic acid forms as a result of the anaerobic metabolism of glucose, damaging brain tissue [13].

Time-dependent Cox regression showed that the covariate recurrent stroke risk was affected by time and age. Stroke patients of ≥ 60 years were found to have a high risk of recurrent stroke for 15 months (HR 1.03). After 15 months, however, the risk was seen

to reduce for this age group. Although a stroke can occur at any age, the risk increases with age, due largely to the artheriosklerosis process and hypertension. These findings differ slightly from those obtained by Supriyadi (2012), who found that patients aged $\geq$ 60 years had a 1.4 times higher risk of recurrent stroke than those aged <60 years. Several studies have shown that recurrent strokes are more common in the elderly; Hankey et al. (1998) found, for instance, that those aged 75–84 years at the time of the first stroke have a 2.6 times higher risk of stroke recurrence.

Stroke patients who are overweight have a high risk of recurrent stroke (HR 1.96). The risk of stroke recurrence for obese patients is also high (HR 3.38). Obesity triggers a process connected with hypertension, hyperlipidemia, and diabetes mellitus. Research conducted by Kurt et al. has shown that individuals with a Body Mass Index (BMI) of <22 kg / m^2 and> 22 kg / m^2 are 1.84 times more likely to suffer from ischemic stroke and 1.93 times more likely to experience hemorrhagic stroke (in Junaidi 2005). Obesity is a condition in which the BMI is $\geq$ 30 kg/m^2, and is a predisposing factor for cardiovascular disease and stroke. This is because the state of obesity is associated with high blood pressure and high blood sugar levels. If someone is overweight, the heart has to work harder to pump blood through the body, thus increasing blood pressure. In addition, obesity can also accelerate the process of atherosclerosis in adolescents and young adults. As such, weight loss can reduce the risk of stroke [8].

4. CONCLUSION

It can be concluded that age, hypertension, obesity, and irregular control influence the recurrence of strokes. In this study, 45.8% of patients experienced recurrent stroke. The average survival period after the occurrence of recurrent stroke was 38 months, with the median survival period being 25 months. The patients who did not undergo regular control treatment after the first attack were 8.7 times more likely to suffer another stroke. The incidence of recurrent stroke before 15 months was higher for those who were overweight and obese (HR = 1.96 and 3.38), and for those who had developed pre-hypertension (HR = 2.26). Additionally, observations after 15 months showed that levels of grade 1 and grade 2 hypertension had increased (HR = 2.86 and 2.07).

5. RECOMMENDATIONS

The Ministry of Health, Jakarta Provincial Health Office, and RSPON need to develop stroke-prevention programs in the community. Post-stroke health checks should also be carried out routinely at clinics or Posbindu PTMs in each region. A program should be developed to enable doctors to visit stroke patients, anda stroke community association should be put into place in each region. In addition, seminarsand education sessions about strokesneed to be offered to local communities.

Finally, research into recurrent stroke must continue. In particular, additional risk factors (such as smoking, diabetic mellitus control levels, the severity of the stroke, the history of stroke within the family, levels of medication adherence, alternative treatments, socioeconomic factors, and levels of family support) must be researched in more detail to help prevent stroke incidence from increasing further.

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