COMPARISON OF CLOPIDOGREL AND ACETOSAL IN THE PREVENTION OF RECCURENT ISCHEMIC STROKE AT DR. MOEWARDI REGIONAL GENERAL HOSPITAL

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ABSTRACT

Objective: This study was conducted to determine the effect of clopidogrel on the prevention of recurrent stroke.

Methods: This study used case–control study; data were taken from patient's medical record of DR. Moewardi Regional General Hospital in the period of January 2013 – February 2017. Case group is a recurrent stroke patient receiving an acetosal or clopidogrel. The control group is a nonrecurrent stroke patient who receives an acetosal or clopidogrel.

Results: During the period of study, the number of medical sample record data are 177 samples from the entire study subjects that met the inclusion and exclusion criteria, 50 medical records entered as subject of case study, 32 medical record samples was excluded because medical record data at the first stroke was gone (obselete), 35 medical record was excluded because medical record data at first stroke was not at of DR. Moewardi Regional General Hospital, 4 samples of medical records was excluded for using a combination of acetosal and clopidogrel, 55 samples of medical records as control subjects. Patients who use clopidogrel have a tendency to prevent recurrent stroke, but statistically not significantly different. This study shows that men tend to suffer more recurrent ischemic stroke (64.0%) than women. While in the control group of recurrent ischemic stroke of women (56.4%) more experienced the first stroke than men. Patients who had a stroke almost all had a history of hypertension (90.2%). Recurrent stroke patients in this study almost all had a history of hypertension. Bivariate analysis was showed that gender, history of diabetes mellitus (DM) and history of hypertension had an effect on recurrent stroke events. From the multivariate analysis, it was found that men had a risk of 2.328 for recurrent stroke (p=0.047), the history of DM had a risk of 3.975 times for recurrent stroke (p=0.016) and history of hypertension was 4.021 times for recurrent stroke (p=0.03).

Conclusion: Clopidogrel has no effect on recurrent stroke. Male, history of DM and hypertension has an effect on recurrent stroke events.

Keywords: Recurrent stroke, Clopidogrel, Medical record, Case–control.

INTRODUCTION

Stroke is the leading cause of disability. In the developed world countries, stroke is the third cause of death [1]. There is an increase in stroke prevalence from 8.3/1000 population to 12.1/1000 population. The prevalence of stroke in Indonesia based on diagnosis by health worker is 7.0 per mile and based on diagnosis by health worker or with symptoms 12.1 per mile. The prevalence of stroke is similar in males and females. The prevalence of stroke in Central Java increased from 5.70/00 (2007) to 7.70/00 (2013) (based on diagnosis by health worker) and 7.6‰ (2007) to 12.30/00 (2013) [2].

Each year approximately 795,000 people suffer from the first stroke or recurrent stroke. Approximately, 610,000 of them for the first stroke and 185,000 for recurrent stroke [3]. A recurrent stroke probability after the first stroke is more than 3% to 10% in the 1st month and 5% to 14% in the 1st year [1]. Research in Singapore showed a recurrent stroke risk is 18.4% after 5 years of the first stroke. Male patients have a higher risk and increased mortality in ischemic stroke [4].

Four antiplatelet drugs have been approved by the Food and Drug Administration (FDA) for prevention of vascular events among patients with a stroke or transient ischmeic attack (TIA): Aspirin, combination aspirin/dipyridamole, clopidogrel, and ticlopidine. On average, these agents reduce the relative risk of stroke, myocardial infarction (MI) or death by about 22% [5]. Antiplatelet therapy is an antithrombotic cornerstone for ischemic secondary prevention and should be used in noncardioembolic stroke therapy. The antiplatelet agents currently used are acetosal, clopidogrel, and acetosal plus extended release dipyridamole American Stroke Association (ERDP-ASA), which is the first-line antiplatelet agent [6]. Clopidogrel is superior to acetosal in preventing death and cardiovascular events after acute noncardioembolic stroke ischemic [7]. Clopidogrel proven as a safe and effective drug for the prevention of secondary vascular events in Clopidogrel Versus Acetosal in Patients at Risk of Ischaemic Received Events (CAPRIE) study, where the benefits of clopidogrel better than acetosal in the prevention of vascular events with a relative risk (RR) reduction 8.7% [8]. Acetosal is the most widely used antiplatelet agent, which according to the study can reduce the RR of recurrent vascular events from 22% to 13% and the risk of recurrent stroke by 15% compared with placebo [1].

METHODS

Materials
Medical records of JKN (National Health Insurance) patients with diagnosis of ischemic stroke in the inpatient room of Dr. Moewardi Regional General Hospital in the period of January 2013 – February 2017 using clopidogrel and using other than clopidogrel (acetosal), medical records of recurrent ischemic stroke patients, with the previous stroke (first stroke) treated at Dr. Moewardi Regional General Hospital.

Methods
The selected research design is case–control study. Retrospective data retrieval was performed through patient medical records with recurrent ischemic stroke using clopidogrel and using other than clopidogrel

(acetosal) in inpatient room of Dr. Moewardi Regional General Hospital in the period of January 2013 – February 2017.

RESULTS

During the period of study, the number of medical sample record data are 177 samples from the entire study subjects that met the inclusion and exclusion criteria, 50 medical records entered as subject of case study, 32 medical record samples were excluded because medical record data at the first stroke were gone (obselete), 35 medical record was excluded because medical record data at first stroke was not at of Dr. Moewardi Regional General Hospital, 4 samples of medical records was excluded for using a combination of acetosal and clopidogrel, 55 samples of medical records as control subjects. Characteristics of study subjects including age and sex. Characteristic of subject study can be seen in Table 1 and frequency types of complications of disease can be seen in Table 2.

Table 1: Distribution of characteristic frequency and disease in clopidogrel patients and patients of asetosal users at Dr. Moewardi Regional General Hospital, January 2013 to February 2017

S. No.	Variable	n (%)	
		Case	Control
1	Age (years)		
	18-59	24 (48.0)	31 (56.4)
	≥60	26 (52.0)	24 (43.6)
2	Gender		
	Male	32 (64.0)	24 (43.6)
	Female	18 (36.0)	31 (56.4)
3	Antiplatelet usage		
	Clopidogrel	16 (32.0)	21 (38.2)
	Asetosal	34 (68.0)	34 (61.8)
4	Hypertension history		
	Yes	46 (90.2)	42 (76.4)
	No	4 (8.0)	13 (23.6)
5	DM		
	Yes	15 (30.0)	7 (12.7)
	No	35 (70.0)	48 (87.3)
6	Hypercolesterolemia history		
	Yes	6 (12.0)	4 (7.3)
	No	44 (88.0)	51 (92.7)
7	Heart disease history		
	Yes	14 (28.0)	12 (21.8)
	No	36 (72.0)	43 (78.2)
8	Period of sick (months)		
	<3	12 (24.0)	-
	≥3	38 (76.0)	-

DM: Diabetes mellitus

The goal of stroke management, in general, is to reduce morbidity and reduce mortality and decrease disability rates. One of the most important attempts to achieve this goal is the early recognition of stroke symptoms and early stroke management starting with rapid and precise pretrial handling. The use of antihypertensive drugs, antidiabetes melitus, antihiperkolerterol, and cardiovascular drugs in patients with ischemic stroke in inpatient at Dr. Moewardi Regional General Hospital can be seen in Table 3.

The American Heart Association (AHA) and the ASA published guidelines to prevent recurrent stroke in patients who have had a previous stroke or TIA. Guidelines for modifying recurrent stroke risk factors include treatable vascular risk factors and modifiable behavioral risk factors, and antithrombotic use (antiplatelet, oral anticoagulant) [9]. Four antiplatelet drugs have been approved by the US FDA to prevent vascular events in patients with stroke or TIA: Acetosal, ticlopidine, clopidogrel, and combinations of acetosal/dipyridamole. On average, antiplatelet agents have been shown to reduce the RR of stroke, MI, About 22% [5]. In this study, used 2 antiplatelet are asetosal and clopidogrel. To see the effect of using clopidogrel with acetosal on prevention of recurrent stroke can be seen in Table 4.

Result of research was conducted at Dr. Moewardi Regional General Hospital, in recurrent ischemic stroke patients where at first stroke using antiplatelet therapy clopidogrel or asetosal can be seen in Table 4. These data were obtained from the medical records of stroke nonhemorrhagic stroke patients from January 2013 to February 2017. Clopidogrel had a risk in preventing recurrent stroke with odds ratio (OR)=0.76. However, statistically did not differ significantly (p=0.508).

The effect of confounding variables on recurrent stroke events can be seen in Table 5 to determine the effect of confounding variables on the incidence of recurrent stroke Chi-square test to show the magnitude of risk. The magnitude of influence is expressed by the OR for bivariate analysis. The value of OR>1 and the trust range does not include the number 1, meaning that the variable is considered a risk factor. The meaning limit is when P≤0.05 with 95% confidence interval (CI).

Confounding variables that are recurrent risk factors for stroke are history of hypertension, history of diabetes, history of hypercholesterolemia, history of heart disease and sex. However, statistically significant between case and control groups was the presence of a history of diabetes and sex.

Age
The study showed that the number of patients aged 18-59 years had a smaller risk for recurrent stroke compared to age ≥60 years. The p value in the analysis of age relationship with recurrent stroke incidence was 0.437 (p>0.05), so it showed that there was no significant relationship between age and recurrent stroke incidence.

Table 2: Frequency types of complications of disease in recurrent ischemic stroke patients at Dr. Moewardi Regional General Hospital, the period January 1, 2013 to February 2017

S. No.	Jenis komplikasi penyakit	Number of cases	Number of control
1	No complication	0	10
2	Hypertension	23	27
3	DM	2	1
4	Hypertension + DM	7	3
5	Hypertension + hypercholesterol	4	2
6	Heart disease	0	1
7	Hypertension + heart disease	7	7
8	DM+heart disease	1	1
9	Hypertension + DM + heart	4	1
10	Hypercholesterol + heart disease	1	0
11	Hypertension + hypercholesterol + heart disease	0	1
12	Hypertension + DM+hypercholesterol + heart disease	1	1

DM: Diabetes mellitus

Gender

Based on the results of this study, men have 2.296 times the risk of recurrent stroke. The results of the analysis found a significant relationship between gender with recurrent stroke incidence with the value p=0.05 (*p≤0.05).

Hypertension history

The result of analysis of correlation between history of hypertension with recurrent stroke incidence showed that patient with a history of hypertension had a risk of recurrent stroke 3.560 times. The association between history of hypertension and recurrent stroke incidence was statistically significant with p=0.03 (*p≤0.05).

Table 3: Distribution of frequency of drug usage of clopidogrel user, asetosal user patient at Dr. Moewardi Regional General Hospital, the period January 2013 to February 2017

S. No.	Variable	n (%)	
		Case	Control
1	Hypertension therapy		
	Yes	35 (70.0)	28 (50.9)
	No	15 (30.0)	27 (49.1)
2	DM therapy		
	Yes	13 (26.0)	10 (18.2)
	No	37 (74.0)	45 (81.8)
3	Hypercholesterol therapy		
	Yes	24 (48.0)	19 (34.5)
	No	26 (52.0)	36 (65.5)
4	Heart disease therapy		
	Yes	14 (28.0)	7 (12.7)
	No	37 (72.0)	48 (87.3)

DM: Diabetes mellitus

Diabetes mellitus history

This study showed that the history of diabetes mellitus (DM) at risk of 2.939 times the incidence of recurrent stroke. Based on the results of the analysis, there is a significant relationship between history of DM with recurrent stroke with p=0.03 (*p≤0.05).

Hypercholesterolemia history

The results of this study indicate that the history of hypercholesterolemia has a risk of 1.739 times the incidence of recurrent stroke. Based on the results of the analysis, there was no significant relationship between history of DM with recurrent stroke incidence with value p=0.410 (p>0.05).

Heart disease history

History of heart disease has a risk of recurrent stroke events 1.394 times. This relationship is not statistically significant with p=0.464 (p≥0.05).

Multivariate analysis was performed to determine the effect of several variables on the incidence of recurrent stroke, then multivariate logistic regression test was done. A multivariate variable that has a value of p<0.05. From the result of the bivariate test above variable having p<0.05 ie gender *p=0.05, history of hypertension *p=0.03, history of DM *p= 0.03.

Confounding variables (male gender, age, history of hypertension, history of DM, history of hypercholesterolemia, and cardiac arrest), multivariate analysis showed three variables that had an effect on recurrent stroke incidence of sex with *p=0.047 (OR=2.328), history of hypertension with *p=0.03 (OR=4.021), and history of DM with indigo *p=0.016 (OR=3.975). The multivariate logistic regression analysis results are available in Table 6.

Table 4: The effect of clopidogrel or acetosal antiplatelet use on the prevention of recurrent stroke occurrence at Dr. Moewardi Regional General Hospital, January 2013 to February 2017

Variable	n (%)		p	OR	95% CI
	Kasus	Kontrol			
Using antiplatelet clopidogrel	16 (32.0)	21 (38.2)	0.508	0.762	0.340-1.705
Not using clopidogrel (asetosal)	34 (68.0)	34 (61.8)			

OR: Odds ratio, CI: Confidence interval

Table 5: The effect of confounding variables against the prevention of recurrent stroke occurrences

Variable	n (%)		p	OR	95%CI
	Case	Control			
Gender					
Male	32 (64.0)	24 (43.6)	0.05	2.296	1.047-5.038
Female	18 (36.0)	31 (56.4)			
Age (years)					
18-59	24 (48.0)	31 (56.4)	0.437	0.715	0.331-1.542
≥60	26 (52.0)	24 (43.6)			
Antiplatelet theraphy					
Using clopidogrel	16 (32.0)	21 (38.2)	0.715	0.74	0.331-1.653
Not using clopidogrel (asetosal)	34 (68.0)	34 (61.8)			
Hypertension history					
Yes	46 (90.2)	42 (76.4)	0.03	3.560	1.076-11.773
No	4 (9.8)	13 (23.6)			
DM history					
Yes	15 (30.0)	7 (12.7)	0.03	2.939	1.084-7.967
No	35 (70.0)	48 (87.3)			
Hypercholesterolemia history					
Yes	6 (12.0)	4 (7.3)	0.410	1.739	0.461-6.560
No	44 (88.0)	51 (92.7)			
Heart disease history					
Yes	14 (28.0)	12 (21.8)	0.464	1.394	0.573-3.390
No	36 (72.0)	43 (78.2)			

OR: Odds ratio, CI: Confidence interval, DM: Diabetes mellitus

Table 6: Multivariate logistic regression test result influence of clopidogrel, history of DM, hypertension and sex on prevention of recurrent stroke occurrence at Dr. Moewardi Regional General Hospital, January 2013 to February 2017

Variables	OR	p	95% CI
DM history	3.975	0.016	1.298-12.170
Gender	2.328	0.047	1.010-5.367
Hypertension history	4.021	0.030	1.142-14.162

OR: Odds ratio, CI: Confidence interval, DM: Diabetes mellitus

DISCUSSION

Characteristics of age-based samples included in the inclusion criteria in this study were adult patients aged from 18 years. The division of this group is based on a group of adult nonelderly and elderly patients. This study shows that recurrent ischemic stroke cases are slightly more prevalent at age over 60 years (52.0%). While on control of ischemic stroke is not repeated (first stroke) more occur at age 18-59 years (56.4%).

This study shows that men tend to suffer more recurrent ischemic stroke (64.0%) than women. While in the control group of recurrent ischemic stroke of women (56.4%) more experienced the first stroke than men. This study is in accordance with research conducted by Siswanto that the incidence of recurrent stroke more experienced by men [9].

Patients who had had a stroke almost all had a history of hypertension (90.2%). Recurrent stroke patients in this study almost all had a history of hypertension. Similarly, in the control group, in which more stroke patients had a history of hypertension (76.4%) than those who did not have a history of hypertension.

According to a British study of TIA, there is a relationship between blood pressure and recurrent stroke. Data suggest that a drop in diastolic pressure of 5 mmHg is associated with a decreased risk of a third of stroke events [10].

The number of patients who had a history of hypercholesterolemia in both case and control groups was fewer. Stroke patients in both recurrent and nonrecurring groups had a history of DM. This is not consistent with studies in the CAPRIE study where patients with DM more in patients with ischemic stroke [11].

This study showed that the number of patients with a history of heart disease was lower in both case and control groups. This is consistent with a study conducted by Moroney *et al.*, in which fewer recurrent stroke patients had a history of heart disease [12].

The time interval between the first stroke and recurrent stroke in this study revealed that larger recurrent strokes occurred over 3 months after the first stroke. This is consistent with a study conducted by Moroney *et al.* that more recurrent strokes occur early in the 90 days after the first stroke compared to 30 days after the first stroke [12].

This study showed that more patients were taking hypertension drugs than those who did not use hypertension drugs in both case and control groups. While the use of drugs diabetes melitus, hypercholesterol drugs and cardiovascular drugs are less used both in case and control groups.

The risk of secondary vessel disease has been shown to decrease with the treatment of hypertension, hypercholesterolemia, and antiplatelet drug therapy [13]. In general, hypertension is the most significant risk factor for stroke, both ischemic and hemorrhagic. Increased blood pressure plays an important role in the development of vascular disease, including coronary heart disease, heart failure, aortic atherosclerosis, cerebral arteries, and small occlusion. Controlling blood pressure

reduces the risk of coronary disease and stroke. A meta-analysis of randomized controlled trials of antihypertensive therapy after stroke or TIA decreased recurrence of stroke (RR=0.76; 95% CI 0.63-0.92) [13].

Stroke (especially ischemic stroke, not hemorrhagic stroke) is a form of hypertension associated with organ damage. Achieving a target of blood pressure reduction in patients with ischemic stroke is considered a major modality to reduce the risk of stroke [6]. Hypertension is a major risk factor for the occurrence of the first stroke or the next stroke [14]. Achieving a target of blood pressure reduction is essential to reduce cardiovascular events in hypertensive patients [15]. Hypertension therapy is used to lower blood pressure and prevent the complications of other diseases associated with high blood pressure [16].

This study showed that recurrent stroke incidence in the group taking antiplatelet clopidogrel therapy was less than the group using the antiplatelet therapy of 32% and 68.0%. While in the control group using klopidogrel 38.2% and who use the assetosal 61.8%. Patients taking antiplatelet clopidogrel therapy showed an OR of 0.762. This means that klopidogrel prevents recurrent stroke events. However, statistically the results were not significantly different (OR=0.762, 95% CI 0.340-1.705, p>0.05) so that clopidogrel is not better in preventing recurrent stroke incidence compared to acetosal in RSUD Dr. Moewardi Surakarta. This is not in accordance with research in the CAPRIE study where the results obtained that klopidogrel more effective than asetosal in reducing the risk of ischemic stroke, MI, and vascular death [11]. This is probably due to differences in therapeutic responses due to differences in the characteristics of the research samples that the researchers did with the samples in the CAPRIE study, and the sample studies were less numerous.

Antiplatelet agents have been shown to reduce the RR of stroke, MI about 22% [5]. Clopidogrel proved to be a safe and effective drug for the prevention of secondary vascular events in CAPRIE study. These trials, the benefits of clopidogrel are better than those for acetosal prevention of vascular events with a RR reduction of 8.7% [8]. A large multinational test (prevention regimen for effectively avoiding second strokes) that compares acetosal plus ERDP with clopidogrel to the risk of recurrent stroke is no different for both antiplatelets, but a better tolerance clopidogrel where less bleeding and headache occur [17]. Clopidogrel is superior to acetosal in preventing death and cardiovascular events after acute noncardioembolic stroke ischemic [18].

Clopidogrel acts on platelets irreversibly by binding to adenosine diphosphate (ADP) receptors, blocking the activation of ADP-dependent activation of the glycoprotein IIb-IIIa complex. This complex acts as a fibrinogen receptor on the platelet surface. Clopidogrel is a P2Y12 receptor antagonist, inhibiting platelet aggregation [19]. The AHA/ASA and American College of Chest Physicians guidelines recommend a daily dose of clopidogrel for secondary stroke prevention is 75 mg [20]. Clopidogrel should be metabolized first by the cytochrome P450 (CYP450) enzyme to produce an active metabolite. Genetic polymorphism CYP450 2C19 causes decreased active metabolites, pharmacokinetic karaketristik differences, and decreases clinical response in patients with poor metabolizers [21]. Patients with high on-treatment platelet reactivity or genetic variations, such as CYP 2C19 loss-of-function alleles, have an increased risk of ischemic events, particularly stent thrombosis. Ethnic groups, with a higher frequency of single nucleotide polymorphisms responsible for clopidogrel resistance, may be benefited from prior genetic testing [22]. Clopidogrel's safety equals to acetosal on moderate doses and is safer than that of teclopidine. It is profitable based on benefit/security ratios. Clopidogrel is an effective antiplatelet agent for use in atherothrombotic disease. According to the study, clopidogrel (CAPRIE) study was superior to acetosal with a RR reduction of stroke incidence of 7.3%, mean annual incidence rate of stroke in clopidogrel group was 7.15% compared to 7.71% [11]. Research profile of hemostasis between clopidogrel and assetosal did not show any significant difference (PT, aPTT and INR). Administration of DLBS1033 at a dose of 3 mg × 490 mg

daily for 90 days on ischemic stroke subjects is safe and comparable to aspirin 80 mg daily or clopidogrel 75 mg daily. There are no significant parameters of hemostasis parameters. No adverse events of bleeding in any group were observed during the study [23].

The occurrence of recurrent stroke is influenced by many factors not only influenced by antiplatelet delivery factor. Therefore, this study also performed the analysis of confounding variables as a recurrent stroke risk factor in both study groups. Confounding variables that are recurrent risk factors for stroke are history of hypertension, history of diabetes, history of hypercholesterolemia, history of heart disease and sex. However, statistically significant between case and control groups was the presence of a history of diabetes and sex.

The age variable in this study showed that there was no significant correlation between age and recurrent stroke incidence. These results are consistent with the research conducted by Burn *et al.* [24], i.e., the risk of recurrent stroke seems to have no association with age, but age is a prognostic factor in recurrent stroke of 75-84 years [25].

Based on the results of this study, men had a risk of 2296 repeated stroke events, statistically significant. This is not in accordance with the research by Burn *et al.* that there is no increased risk of recurrent stroke in men [24].

The history of hypertension has a risk of recurrent stroke 3.560 times, statistically significant (*p≤0,05). This is in accordance with research conducted Burn *et al.* that hypertension increases the risk of recurrent stroke 1.01 times [24]. Thomas *et al.*'s study also showed similar results that hypertension increased the risk of recurrent stroke 1.40 times [26].

Acute hypertension is an increase in blood pressure above normal values and is the initial premorbid which occurs within the first 24 hrs of symptom onset in stroke patients. This phenomenon is reported in >60% of patients with stroke in a representative national study of the United States [27].

Increased blood pressure is associated with increased intracranial pressure (ICP), especially in the presence of brainstem compression. Where it has particular relevance for patients with intracerebral and subarachnoid hemorrhage. Increased ICP can lead to increased blood pressure. However, high blood pressure does not clearly show brain ischemia. This suggests that a major cause of acute hypertensive responses is the damage or compression of certain regions of the brain that mediate autonomic control [27].

This study showed that the history of DM had a risk of 2.939 times the incidence of recurrent stroke, statistically significant. This is consistent with the study conducted by Zavoreo patients with DM had a 1.5-3 stroke risk compared with patients with no history of DM related to increased mortality and morbidity of the disease [28]. In accordance with the results of the CAPRIE study in which DM increased the risk of ischemic stroke more than 3-fold compared with no DM [11]. The condition of hyperglycemia can increase stroke severity and also worsen the clinical outcome of stroke [29].

The results of this study indicate that the history of hypercholesterolemia has a risk of 1.700 times the incidence of recurrent stroke is not statistically significant. This is not consistent with studies in the CAPRIE study that hypercholesterolemia increases the risk of ischemic stroke 4-fold higher [11]. Hyperlipidemia is not a potential risk factor for stroke when compared with the risk of heart disease. Although, the risk of stroke decreases with the use of statins in patients with coronary artery disease [13].

Confounder variables (male gender, history of hypertension, history of DM) were done multivariate analysis showed three variables that have an effect on the occurrence of repetitive stroke that is gender and history of DM and history of hypertension. This study shows that men have a higher risk for recurrent stroke than women. This is not

consistent with the research by Burn *et al.* that there is no increased risk of recurrent stroke in men [24]. A history of DM and a history of hypertension also had an effect on recurrent stroke events. This study is in accordance with research conducted by Spurthi, *et al.* the main risk factor in stroke patients is hypertension followed by diabetes [30]. And also this study is in accordance with research conducted by Vurumadla *et al.* that the risk factors associated with stroke is hypertension followed by diabetes [31].

The percentage of occurrence of recurrent stroke after the first major stroke occurred in patients with cardiac complications with cholesterol (100%), complications of hypertension, DM with heart (80%), complication history of hypertension with DM (70%), and history of DM (66.7%). The percentage of recurrent stroke in people with DM (66,7%) is bigger than in hypertension patient (46%).

CONCLUSION

Clopidogrel has no effect on recurrent stroke. Male and history of DM, history of hypertension have an effect on recurrent stroke events.

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