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Risk factors of intracranial stenosis among older adults with acute ischemic stroke

Rizaldy Pinzon*, Laksmi Asanti*, Sugianto*, and Kriswanto Widyo*

ABSTRACT

*Neurology Department,
Bethesda Hospital, Yogyakarta

Correspondence
[a]dr. Rizaldy Pinzon
Neurology Department,
Bethesda Hospital, Yogyakarta
Email:
medidoc2002@yahoo.com

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Intracranial large artery atherosclerosis is an important cause of stroke worldwide. Previous studies have shown that it is found more commonly in Asians. However, studies of intracranial stenosis in Indonesian stroke patients have been very few in number. The aim of this cross-sectional study was to determine the frequency and risk factors of intracranial stenosis in acute ischemic stroke. The data were obtained from 234 consecutive patients in the transcranial doppler (TCD) registry. Documentation of risk factors was performed systematically and for TCD sonography TD-DOP 9000 equipment with a 2-MHz probe was used for the examination of the intracranial circulation. The criteria of middle cerebral artery (MCA) stenosis used in this study were a peak systolic velocity (PSV) >140 cm/s or mean systolic velocity (MSV) >80 cm/s. For stenosis of the posterior circulation the criteria were PSV > 90 cm/s or MSV >60 cm/s. The data were obtained from 234 patients, and complete examinations were performed in 182 patients (77.7%). Ischemic stroke is the most common indication for performing TCD sonography. Stenosis was present in 38% of cases, with stenosis iof the anterior circulation being the more common. The most frequent risk factors were hypertension, dyslipidemia, and diabetes. Intracranial stenosis is common in stroke patients, in whom the risk factors are hypertension and diabetes**.**

Keywords: Stenosis, intracranial, risk factor, acute ischemic stroke

INTRODUCTION

Stroke is the leading cause of mortality and disability, and may be caused by either modifiable or non-modifiable risk factors. It is the third leading cause of death and disability among adults. The incidence of stroke has continued to increase since the mid-1960s, with up to 700,000 new cases being reported in the United States each year.[1,2] Intracranial arterial stenosis is a significant risk factor for vascular events, having been implicated as a causal factor in 8% to 10% of all ischemic strokes[3] and as a major factor in recurrent stroke and

vascular mortality.[4,5] An important cause of intracranial arterial stenosis is intracranial atherosclerosis.[6,7] Atherosclerosis is a systemic, multifocal disease with various signs and symptoms, caused by atherosclerotic lesions in the arterial tree. In the brain the lesions may be located in the extracranial carotid or intracranial arteries.[8-10] Effective preventive measures are needed for preventing stroke and its recurrence.[6,11]

Symptomatic atherosclerotic intracranial stenosis accounts for approximately 10% of ischemic strokes. Risk of stroke in patients with middle cerebral artery (MCA) stenoses was reported to be around 24% during a 6-year follow-up study. The cerebral hemodynamic study and its alterations may be a good indicator for long-term outcome.[12] Previous studies have caused some controversies about the risk factors of intracranial stenosis.[8,9] Increasing lood pressure, increasing blood cholesterol, and atrial fibrillation are definite causal risk factors for ischemic stroke because randomized controlled trials (RCTs) have shown that treating them reduces the incidence of ischemic stroke.[13-15] Cigarette smoking, diabetes mellitus, ischemic heart disease, and valvular heart disease are probably also causal risk factors for ischemic stroke because epidemiological case-control and cohort studies have shown that these characteristics are significantly associated with an increased risk of stroke; moreover, the association is strong, consistent among studies, biologically plausible, and independent of other factors that were measured and analyzed. However, it is possible that these associations are confounded by other factors that have not been measured and analyzed in epidemiological studies uncontrolled confounding.[16-17] A study in Surabaya showed that out of the 675 intracranial arterial segments examined, 118 (17%) segments had stenosis of more than 29% or had occlusion on digital subtraction angiography (DSA).[18] There are only a few studies about intracranial stenosis in Indonesia. The aim of this study was to determine the frequency and risk factors of intracranial stenosis in acute ischemic stroke.

METHODS

Research design

In this cross-sectional study, we examined 234 consecutive patients undergoing transcranial doppler (TCD) studies. Further evaluation was performed for acute stroke patients with symptoms of obstruction in anterior or posterior cerebral artery territories. Patients with a TCD diagnosis of intracranial stenosis were further evaluated.

Data collecting

The recorded data consisted of demographic characteristics, risk factors and tests results. Hypertension was defined as a history of elevated blood pressure (systolic blood pressure >140 mmHg or diastolic blood pressure >90 mmHg) in two separate recordings or elevated blood pressure before admission that required antihypertensive medications. Diabetes mellitus was defined as a history of elevated blood glucose in two separate tests (fasting level >125 mg/dl) or diabetes treated with medication before admission. Hyperlipidemia was defined as history of an abnormally high lipid level that required either dietary or pharmacologic intervention. Smoking was documented by quantity-frequency assessment at the time of admission.

Measurements

TCD sonography is a non-invasive, non-ionizing, inexpensive, portable and safe technique that uses a pulsed Doppler transducer for assessment of intracerebral blood flow**.** The

purpose of this test is to detect any narrowing or blockage in these arteries that may decrease or stop the flow of blood to the brain. A small hand-held, wand-like probe covered with a conductive gel will be placed and held at various areas on the head of the subject, usually at each temple, over each eye, and at the base of the skull. This enables the examiner to image the blood flow in the arteries and to record the flow in each artery. The procedure should take 20 to 60 minutes and is painless.[19,20]

TCD studies of intracranial vessels were performed by TDOP-TC9000P unit with a 2-MHz probe for the examination of intracranial circulation. MCA was designated as stenotic if its peak systolic velocity was greater than 140 cm/s or its mean velocity exceeded 80 cm/s.[21] A diagnosis of vertebral segment and proximal basilar artery stenosis was made if there were focal increases of the peak systolic and mean velocities to 90 cm/s and 60 cm/s or more.[22]

Data analysis

We used SPSS to save and analyze the data. Independent t-test and chi square test were used to compare the variables.

RESULTS

We analyzed the TCD results of 234 patients from our TCD registry, with mean age of 58.35 years. Complete data were collected for 182 patients (77.7%). The most common reason for incomplete data was poor temporal window and bedridden-ventilated patients. The study sample consisted of 52% males and 48% females. The most common indication for TCD examinations in this study was non-hemorrhagic stroke, which was found in around 58% of the study sample (136 patients), followed by vertebrobasilar insufficiency (Figure 1).

The results of the TCD studies in ischemic stroke patients is presented in Figure 2. The proportions of abnormalities detected were as follows: stenosis (38%), atherosclerosis (30%), and hypoperfusion (21%).

Figure 3 shows stenosis in the right middle cerebral artery. In comparison to the posterior circulation, stenosis in the anterior circulation is more common (Figure 4), and the most frequent sites are the middle cerebral artery and the internal carotid artery siphon.

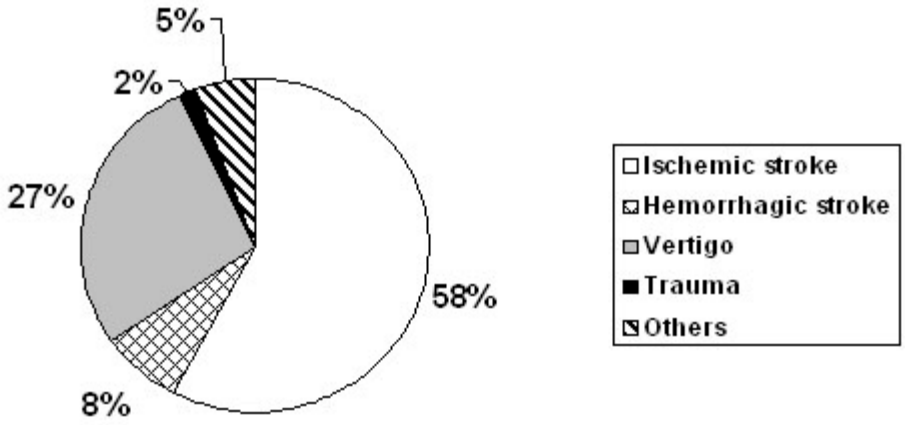

Figure 1. Indications for TCD studies

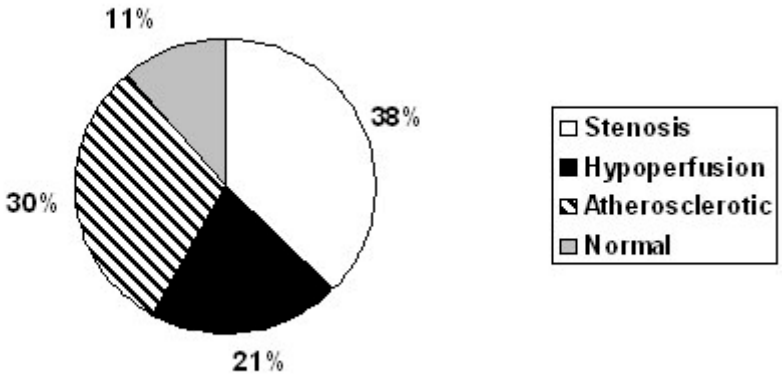

Figure 2. Distribution of abnormalities of TCD studies in patients with acute ischemic stroke

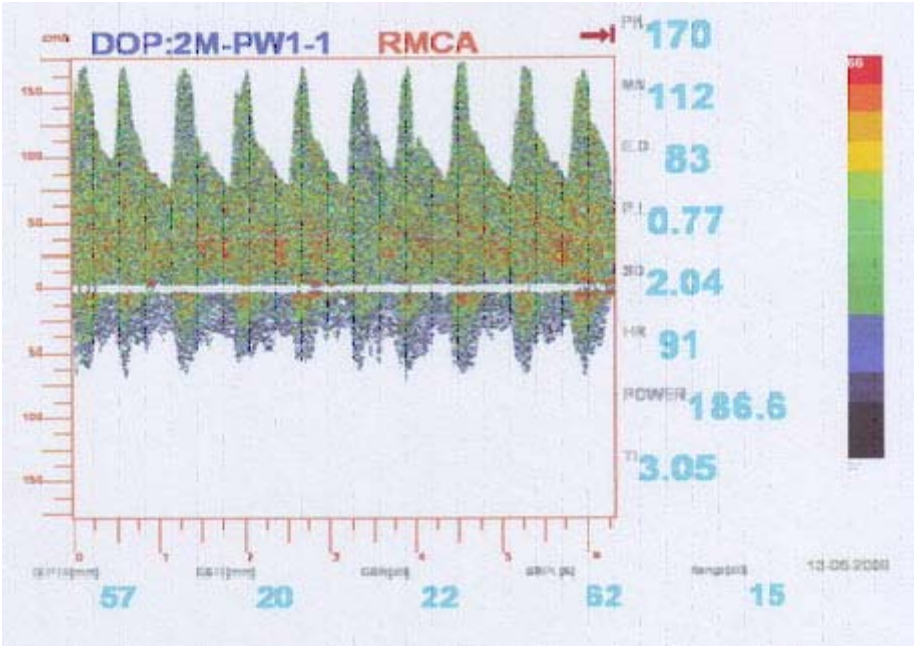

Figure 3. Stenosis in the right middle cerebral artery

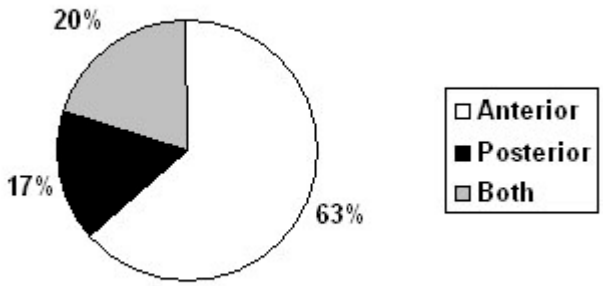

Figure 4. Distribution of sites of the stenosis in patients with intracranial stenosis (52 patients)

Table 1. Frequency of vascular risk factors in stroke patients with intracranial stenosis (n = 52)

Risk factors	Frequency
Age (yrs)	Mean 58.35
Hypertension	72%
Diabetes	24%
Smoking	22%
Dyslipidemia	38%
Age > 60 years old	35%

Table 2. The risk factors of intracranial stenosis in acute ischemic stroke

Risk Factors	OR (95% CI)	p
Male	0.87 (0.55-1.36)	0.53
Hypertension	2.97 (1.76-4.98)	0.01*
Diabetes	1.48 (1.12-2.43)	0.05*
Smoking	1.14 (0.69-1.73)	0.86
Dyslipidemia	1.32 (0.82-1.74)	0.41
Age > 60 years old	1.05 (0.65-1.67)	0.83

We analysed the distribution risk factors in patients with intracranial stenosis, and compared it with ischemic stroke patients without stenosis. The most frequent risk factor for atherosclerosis was hypertension with a frequency of 72%, whilst diabetes mellitus, hyperlipidemia, and smoking had frequencies of 24%, 38%, and 22% respectively. Table 1 presents the frequency of vascular risk factors in intracranial stenosis patients.

There was a significant relationship between hypertension and diabetes with intracranial stenosis. Both hypertension and diabetes increase the risk of stenosis (OR=2.97, 95% CI=1.76-4.98, $p<0.05$ for hypertension, and OR=1.48, 95% CI=1.12-2.43, $p<0.05$ for diabetes).

DISCUSSION

The findings of this study are in agreement with those of previous studies, suggesting that atherosclerotic occlusive lesions are common in Asians.[23-25] In our studies intracranial lesions appeared to be the cause of atherosclerotic occlusive disease in more than around 30% cases. However, this figure may be an overestimation because we excluded patients with poor temporal windows (mostly elderly women), and patients who were moribund with severe stroke (commonly from cardioembolic stroke).

Multiple intracranial stenoses were found frequently, a finding that is in agreement with some other studies.[26,27] Our data showed that MCA was the most frequent stenotic intracranial artery. Despite some previous suggestions, we found no statistical difference in the frequency of intracranial lesions between men and women. However, due to the better trans-temporal windows, we suggest that TCD is a better device for studying intracranial arteries in men. In contrast, results from the Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) trial showed that women have a higher risk for recurrent ischemic stroke and for the combined end point of stroke and vascular death.[28] The explanation for this finding is complex. Women have a greater clustering of risk factors that are indicative of metabolic abnormalities (e.g. high body mass indexes, hypertension, and diabetes) and those that portend increased risk based on sociodemographic features, lifestyle, and family history of stroke. Women may have smaller intracranial arteries than men, which could pose a greater risk for stroke in the territory of a stenotic intracranial artery.[29] An interesting finding in our study is that intracranial stenosis is more frequently

detected in patients with a history of either diabetes mellitus or hypertension. This finding is in agreement with some studies,[12,30] and in disagreement with some others.[8,31] The WASID trial in North America showed consistent results, in which elevated mean SBP and DBP were associated with increased risk of stroke after adjustment for a number of factors. These were age, type of qualifying event (transient ischemic attack versus stroke), gender, body mass index, time from qualifying event, history of diabetes mellitus, history of hypertension, race, percentage of intracranial artery stenosis at study entry, and hyperlipidemia.[32] Although we found no association between the site of the lesion and a history of known lipid disorder, this finding should be interpreted with caution, as blood lipids and lipoprotein concentrations were not systematically measured in our study.

Because we can now detect intracranial occlusive disease safely and reliably with TCD and magnetic resonance angiography (MRA), studies of the prevalence of intracranial stenosis in asymptomatic patients with multiple risk factors is feasible.[33] Identifying patients with asymptomatic intracranial stenosis may enable us to implement preventive measures early in this high-risk population. This is particularly important because limited success of pharmacological interventions in preventing stroke has now been replaced by technological developments offering improved methods for endovascular therapy of cerebral artery stenosis.

CONCLUSIONS

Intracranial stenosis is present in more than one third of ischemic stroke patients. Hypertension and diabetes are significantly more prevalent in intracranial stenosis.

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