Correlation between Framingham risk score and degree of asymptomatic intracranial artery stenosis on stroke prone person

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Abstract. Intracranial artery stenosis is the most frequent cause of ischemic stroke. Yet there is no recommendation for population-based screening with the goal of primary stroke prevention strategies. Framingham risk score D’Agostino’s modification has been shown as highly accurate screening to assess the risk of intracranial artery stenosis that lead to stroke. The aims of study to determine the correlation between Framingham risk score and degree of asymptomatic intracranial artery stenosis among stroke prone person. In the study, 32 patients were included. Intracranial stenosis was assessed by transcranial Doppler (TCD). Stenosis defined if the mean flow velocity (MFV) value was abnormal. Artery stenosis was most common in the left middle cerebral artery (MCA) (34.4%). After multiple linear regression analysis was done, only MFV of right carotid siphon artery (CSA) (p = 0.060; r = -0.493), MFV of left anterior cerebral artery (ACA) (p = 0.073; r = 0.332), MFV of left MCA (p = 0.065; r = 0.341), had significant correlation. The conclusion appears that the stroke risk score has moderate correlation with the degree of asymptomatic intracranial artery stenosis, especially with MFV of right CSA, left ACA and left MCA.

1. Introduction
According to the basic health research on 2013, the prevalence of stroke in Indonesia is 12.1 for 1000 people. The research showed that 76% of patients every year are first-time stroke patients. Preventive intervention could be done as early as possible by identifying stroke prone person [1].

Stenosis of intracranial major arteries is a common cause of ischemic stroke in the world [2]. Intracranial arteriosclerotic is related to old age, hypertension, diabetes mellitus (DM) and dyslipidemia, and its prevalence rises if two or more risk factors are present [3].

The probability of stroke in the upcoming 10 years in a person could be predicted by the Framingham risk score with D’Agostino modification. The variable in the scoring system are age, sex, systolic blood pressure treated or not treated, history of diabetes, heart diseases, atrial fibrillation and left ventricular hypertrophy. The higher score on a person the more likely the person to have stroke.

The most common cause of ischemic stroke is intracranial artery stenosis, but no population-based screening recommendation for intracranial artery stenosis with the purpose of preventing primary stroke is established [4]. Framingham risk score with D’Agostino modification can evaluate the risk of stroke which is mostly caused by intracranial artery stenosis, so this score will play an important role in detecting early intracranial artery stenosis.
The purpose of the research is to determine the correlation between Framingham risk score and degree of asymptomatic intracranial artery stenosis among stroke prone person in Mohammad Hoesin Hospital Palembang, Indonesia.

2. Methods
This study is an analytical observational study with correlation test design. Population of this study is patients that come to the polyclinic (kidney-hypertension, cardiology, endocrinology division) in April-September 2016. The sample of this study is population that met the inclusion and exclusion criteria. The inclusion criteria are; age >54 years old, stroke prone person (patient that is already diagnosed with one or more of these: hypertension, diabetes mellitus, dyslipidemia and heart disease).

The exclusion criteria are history of stroke, transient ischemic attack (TIA), history of head injury, patients difficult to examine TCD, or patient contraindicated for TCD.

After signing a consent form, that stroke risk value is assessed, and then the TCD examination is done. If the patients are proved with stenosis, then the patients are advised to consult to the neurology polyclinic. Then the data is analyzed by the spearman correlation test and lineer regression analysis.

3. Results
There are 32 patients that met the inclusion and exclusion criteria during the period of April-October 2016, most of the patients were female (65, 5%). Twenty three patients (71,9%) have hypertension, 10 patients (31,3%) were active smokers, 11 patients (34,4%) have DM, 15 patients (46,9%) were diagnosed with heart disease, all of the patients have dyslipidemia, 2 patients (6,3%) have kidney disease and 6 patients (18,8%) have history of stroke in the family showed abnormal MFV.

Of all the 32 patients, 5 patients (15,6%) have right carotid syphon artery (CSA) stenosis; 3 patients (9,4%) have left CSA stenosis; 3 patients (9,4%) have right anterior cerebral artery (ACA) stenosis; 4 patients (12,5%) have left ACA stenosis; 3 patients (9,4%) have right middle cerebral artery (MCA); 11 patients (34,4%) have left MCA stenosis; no patients were found to have right posterior cerebral artery (PCA) stenosis; 2 patients (6,3%) have left PCA Stenosis; 4 patients (12,5%) have right vertebral artery (VA) stenosis; 7 patients (21,9%) have left VA stenosis; and 2 patients (6,3%) have basilar artery (BA) stenosis. Stenosis or occlusion on the right and left petrous carotid artery (PCRA) were not found (figure 1).

![Figure 1. Intracranial Artery Characteristic of the research subjects.](image1.jpg)

Risk factor on all the 32 patients is assessed (age >50 years, history of hypertension, DM, smoking, heart disease, kidney disease, and history of stroke in the family). The study showed that the MFV of right MCA on patients with 1 risk factor is 33 (33-33), 2 risk factors is 50 (43-57), 3 risk factors is 58 (33-70) and more than 3 risk factors 53 (35-107) cm/second. Where the MFV of left MCA on patients with 1 risk factor is 61 (61-61), 2 risk factors is 29 (7-51), 3 risk factors is 48 (38-84) and more than 3 risk factors 59,5 (34-93) (table 1).
Bivariate analysis was done to find the correlation between the stroke risk value and the MFV of intracranial arteries using the Spearman method (table 2). This study showed that there is a statistically significant correlation between the stroke risk value and the MFV of the right CSA \((p=0.004)\) with correlation coefficient of \(r=-0.497\). Statistically significant correlation is also shown between the stroke risk value and the MFV of the left CSA \((p=0.004)\) with \(r=-0.491\). After linear regression analysis was done, statistically significant correlation were also found between the stroke risk value and the MFV of intracranial arteries \((r=0.582)\).

### Table 1. Mean Flow Velocity (MFV) value of study subjects.

|                  | Right MFV | Left MFV | Right MFV | Left MFV | Right MFV | Left MFV | Right MFV | Left MFV | Right MFV | Left MFV | Right MFV | Left MFV | Right MFV | Left MFV | Right MFV | Left MFV | Right MFV | Left MFV | Right MFV |
|------------------|-----------|----------|-----------|----------|-----------|----------|-----------|----------|-----------|----------|-----------|----------|-----------|----------|-----------|----------|-----------|----------|-----------|
| Risk Factor 1    | 33 (33-39) | 39 (39-46) | 46 (46-51) | 48 (48-54) | 29 (29-34) | 29 (29-34) | 33 (33-39) | 61 (61-67) | 28 (28-34) | 22 (22-28) | 36 (36-42) | 33 (33-39) | 40 (40-46) |
| Risk Factor 2    | 38 (34-40) | 35 (35-40) | 34 (34-39) | 35 (35-40) | 30 (30-35) | 30 (30-35) | 50 (50-55) | 29 (29-34) | 17 (17-22) | 16 (16-21) | 25 (25-30) | 24 (24-29) | 26 (26-31) |
| Risk Factor 3    | 36 (32-40) | 38 (38-43) | 46 (46-51) | 44 (44-49) | 42 (42-47) | 42 (42-47) | 58 (58-63) | 48 (48-53) | 25 (25-30) | 21 (21-26) | 31 (31-36) | 30 (30-35) | 37 (37-42) |
| More than 3 risk factors | 37 (34-41) | 40 (40-45) | 45 (45-50) | 44 (44-49) | 43 (43-48) | 43 (43-48) | 53 (53-58) | 59 (59-64) | 29 (29-34) | 26 (26-31) | 31 (31-36) | 30 (30-35) | 34 (34-39) |

Positive correlation coefficient was obtained between the stroke risk value and the MFV of the left ACA and the MFV of the left MCA. The analysis also showed that the MFV of the left intracranial arteries were dominating the right. This is possibly because activities performed by most of the study subjects were higher in the left hemisphere compared to the right hemisphere. Left hemisphere’s metabolism is higher compared to the right hemisphere resulting in higher blood flow to the left which increases the risk of atherosclerosis. According to the study done by Feldberg et al, the specificity and sensitivity of TCD is above 50% in identifying intracranial artery stenosis. Cutoff value of 100 cm/s (52%) subject on the MCA, 8 (26%) subjects on PCA and 2 (7%) subjects on the distal internal carotid artery [6].

On the door-to-door TCD survey done in the Chinese villages, 6,9% out of 590 populations above 40 years old who are screened by TCD have intracranial atherosclerosis [7]. In Hong Kong, the prevalence of MCA stenosis detected by the TCD on 3057 asymptomatic patients with at least one risk factor is 12,6% [8]. The prevalence of MCA stenosis increases with the number of risks factor the patients have. On other TCD study, 1,068 Chinese asymptomatic subjects, the prevalence of MCA stenosis is 5,9% [9].

An earlier detection of intracranial atherosclerosis will allow doctors to make an earlier intervention. There are many controversies regarding the degree of MCA stenosis responsible for stroke, some scientist argued according to a small study that MCA stenosis is not very significant in the population of white people. But some post-mortem research showed that there are involvements of MCA atherosclerosis as the cause of stroke. Further study is needed to evaluate and determine the prevalence and significance of MCA diseases as the cause of ischemic injury [10].
MCA is the most common site for embolic stroke, because MCA carry almost 2/3 of blood from ICA and is morphologically the extension of the ICA. Its variability, bifurcation and branches are less compared to other arteries [11].

### Table 2. Bivariate analysis between the risk value of stroke and MFV.

| MFV of intracranial Arteries | r   | p    |
|------------------------------|-----|------|
| Right MFV PCRA              | 0.043 | 0.813 |
| Left MFV PCRA               | -0.450 | 0.806 |
| Right MFV CSA               | -0.497 | 0.004 |
| Left MFV CSA                | -0.491 | 0.004 |
| Right MFV ACA               | -0.093 | 0.612 |
| Left MFV ACA                | -0.044 | 0.812 |
| Right MFV MCA               | -0.122 | 0.506 |
| Left MFV MCA                | 0.194  | 0.288 |
| Right MFV PCA               | 0.001  | 0.995 |
| Left MFV PCA                | 0.055  | 0.764 |
| Right Vertebral MFV         | -0.145 | 0.429 |
| Left Vertebral MFV          | -0.307 | 0.087 |
| Basilar MFV                 | -0.166 | 0.364 |

**Note:** Significant if p < 0.05, CI 95%. r = correlation coefficient, value r < 0.20 = very weak correlation, value r 0.20-0.39 = weak correlation, value r 0.40-0.59 = Moderate correlation, value 0.60-0.79 = strong correlation, r ≥ 0.8 very strong correlation.

Negative correlation coefficient was obtained between the stroke risk value and the MFV of right CSA, this could be due to low MFV but a normal pulsatility index (PI), but still in the normal range (no stenosis). In the major cerebral artery, a typical characteristic of stenosis is: increase of flow velocity, flow disturbances, or co-vibration Phenomena [12].

The weakness of this study is that the dominant hemisphere of the patients is not noted, TCD examination is limited to the large basal arteries and still difficult to assess smaller arteries, hematocrit is not examined, and the viscosity, carbon monoxide and patient’s temperature could influence the result in the TCD examination. The risks of stroke in this research didn’t proportional.

### 5. Conclusion

This study showed that there are correlation between stroke risk value and the degree of asymptomatic intracranial artery stenosis on stroke prone person. TCD examination could be considered for screening asymptomatic intracranial stenosis and further study is needed.

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