The Clinical Outcome Comparison of Ischemic Stroke with and without Ischemic Heart Disease

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Abstract

Aim: Ischemic heart disease and stroke are the leading cause of morbidity and mortality worldwide. Ischemic stroke and ischemic heart disease have similar pathophysiological mechanisms and risk factors. Ischemic heart disease patients are associated with increased morbidity and mortality, but the studies describing outcomes of ischemic heart disease in ischemic stroke patients are lacking. This is the first study to correlate ischemic heart disease in ischemic stroke with length of stay and functional outcome by using modified Rankin Scale (mRS). This study aims to compare the clinical outcome of ischemic stroke patients with ischemic heart disease and without ischemic heart disease.

Methods: This retrospective cohort study of 200 patients were first incident acute ischemic stroke recorded in the Bethesda Hospital Yogyakarta Stroke Registry (2012-2017). These patients were divided into ischemic stroke patients with ischemic heart disease and ischemic stroke patients without ischemic heart disease. The primary outcomes of the study was in-hospital mortality, disability measured by modified Rankin Scale (mRS), and length of stay. The data were analyzed bivariate followed by the Chi-square test and Mann-Whitney.

Results: Data of 200 patients with 100 stroke patients with ischemic heart disease consist of fifty-eight male (58.0%) and eighty-six (86.0%) were more than 50 years old. Compare to 100 stroke patients without ischemic heart disease consist of fifty-eight male (58.0%) and eighty-nine (89.0%) were more than 50 years old. The mortality of stroke patients with ischemic heart disease group is eighteen patients (18.0%), sixty patients (60%) have poor functional outcome (mRS >2) and have length of stay 7.50 (0-40) days. Bivariate analysis showed stroke patients with ischemic heart disease group is significantly associated with higher in-hospital mortality (RR:2.9, 95%CI:1.1–7.3, p<0.019), worse disability (RR:2.6, 95%CI:1.3 –5.1, p<0.005) and prolonged hospital stay (7.50 (0-40) vs 4 (0-14), p<0.001) than in stroke patients without ischemic heart disease group.

Conclusion: Ischemic stroke patients with ischemic heart disease is statistically significantly associated with higher in-hospital mortality, worse disability, prolonged hospitalization than in ischemic stroke patients without ischemic heart disease.

Keywords: ischemic heart disease, ischemic stroke, comparison, clinical outcome

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Introduction
Coronary artery disease (CAD) and stroke are the leading causes of death and disability in patients with cardiovascular disease (CVD). Cardiovascular disease accounts for 31% of all deaths in global. Fifteen million people aged ≥20 years in the United States experience CVD, contributing about 800,000 deaths [1]. CAD victims in Indonesia reached 138,380 or 9.89% of total deaths. The Sample Registration System (SRS) Ministry of Health in the Indonesia in 2014 showed that deaths of CAD were around 12.9%, the second highest position after stroke [2].

Ischemic stroke and ischemic heart disease have similar pathophysiological mechanisms and risk factors [3]. Previous studies have shown an increased risk of ischemic stroke after Ischemic heart disease is highest in the first few days after the event [4]. Stroke following an ischemic heart disease remains a challenge even today, and can lead to potentially poor clinical outcomes. Stroke remains a catastrophic complication of ischemic heart disease with a mortality rate of up to 60% at one year [3, 4].

Ischemic heart disease patients are associated with increased morbidity and mortality [5], but the studies describing clinical outcomes of ischemic heart disease in ischemic stroke patients are a lack. This is the first study to correlate Ischemic heart disease in ischemic stroke with length of stay and functional outcome by using mRS. The understanding of risk factors especially ischemic heart disease can help the clinician for further management. This study aims to compare the clinical outcome of ischemic stroke patients with ischemic heart disease and without ischemic heart disease.

Methods
Design
The design of this study was retrospective cohort that used secondary data recorded in the Bethesda Hospital Yogyakarta Stroke Registry from 2012 until 2017. The primary outcome of the study was in-hospital mortality, disability measured by modified Rankin Scale (mRS), and length of stay. We only used complete data. Incomplete data were excluded from the study. Each subject was followed up from the first day until they were died in-hospital or discharge from the hospital.

Results: First group of 100 patients with ischemic heart disease and ischemic heart disease, from total of 200, contained 58% women and 42% men. The age of patients was 50 years. Second group of 100 patients with ischemic stroke and ischemic heart disease, from total of 200, contained 58% women and 42% men. The age of patients was 50 years. In conclusion, this study is the first study to correlate Ischemic heart disease in ischemic stroke with length of stay and functional outcome by using mRS.
Study population

The study population of this study were first incident ischemic stroke patients at Bethesda Hospital in Yogyakarta that confirmed with clinical and CT (computed tomography) scan of the head. The inclusion criteria were as follows: Ischemic stroke patients and first-time stroke. We excluded patients with a history of previous stroke, onset more than 24 hours and incomplete data. We use OpenEpi software to calculate the sample size with a significance level <0.05 and power 80%. The calculation showed that minimal sample in each group is 30. Subjects were selected in consecutive manner until required subject obtain.

Variables

The dependent variable in this study is in-hospital mortality, disability measured by modified Rankin Scale (mRS), and length of stay. Disability status was defined as limitations in performing activities and on this basis the subjects were differentiated into those poor functional outcome and good functional outcome. Disability status was measured on a modified Rankin score (mRS) scale [6,7]. Subjects with good functional outcome included subjects who were no symptoms, no significant disability and slight disability (mRS score 0,1 and 2). Subjects with poor functional outcome included subjects with moderate disability, moderately severe disability, severe disability with a home care program, and death (mRS score 3 to 6).

The Independent variables were ischemic heart disease. Group divided into ischemic stroke patients with history of ischemic heart disease group and ischemic stroke patients without history of ischemic heart disease group. Ischemic heart disease diagnosis was made based on American Heart Association criteria Ischemic heart disease. Included stable angina pectoris; which was confirmed by cardiac stress test; unstable angina pectoris, ST-elevation myocardial infarction (STEMI), and non STEMI confirmed by electrocardiography (ECG). The data about clinical characteristics profile consist of onset to hospital admission, comorbidities, stroke risk factors, in-hospital complications used for subject characteristics.

| | Ischemic Heart Disease | No Ischemic Heart Disease | p-value |
|---|---|---|---|
| Male | 58 | 58 | 1.000 |
| Age >50 year old | 14 | 11 | 0.521 |
| Early onset (≤ 6 hours) | 46 | 36 | 0.151 |
| Loss of Consciousness | 27 | 13 | 0.013 |
| Comorbid Hypertension | 52 | 49 | 0.777 |
| Comorbid Dyslipidemia | 42 | 33 | 0.189 |
| Comorbid Atrial Fibrillation | 7 | 3 | 0.331 |
| Complication | 20 | 4 | 0.001 |
| Complication Urinary Tract infection | 2 | 0 | 0.497 |
| Complication Pneumonia | 10 | 0 | 0.002 |
| Complication Gastrointestinal bleeding | 10 | 4 | 0.164 |
| Complication Decubitus | 5 | 0 | 0.059 |

The mortality, poor functional outcome, prolonged hospitalization were more common in ischemic stroke patients with IHD group. Based on the results of the bivariate analysis in Table 2 Bivariate analysis showed stroke patients with ischemic heart disease group was significantly associated with higher in-hospital mortality (RR:2.9, 95%CI:1.1 –7.3, p<0.019), worse disability (RR:2.6, 95%CI:1.3 –5.1, p<0.005) and prolonged length of stay (7.50 (0-40) days vs 4 (0-14) days, p<0.001) than in stroke patients without ischemic heart disease group.
Cardioembolic occlusion of a large artery and lack of occlusion have a lower risk of death, which may be associated with cardioembolism and small vessel coagulation activity during ischemic heart disease, persisting at the time of embolic stroke, accounting for up to 30% [13, 14]. Increased disease and myocardial infarction were common cardiac sources to an increased risk of ischemic stroke [10]. Ischemic heart disease was strongly associated with the development of acute ischemic stroke, patients with a history of ischemic heart disease had more than twice the risk of stroke than those who have not [5,9]. Other studies also considered ischemic stroke after ischemic heart disease was an important complication, with a mortality rate of up to 60% at one year [5,8].

Cardiac Injury in ischemic heart disease was associated with higher mortality, worse disability, and prolong hospital stay in acute ischemic stroke patients. This result was also similar to previous studies that cardiac injury may lead to cardiac dysfunction and hypokinesis of cardiac chambers, which in turn may predispose the patient to left ventricular mural thrombus (LVMT) due to flow characteristics in the left ventricle, this LVMT then becomes a potential source of embolic events [10]. Coronary artery disease was associated with significant left ventricular dysfunction, it is an important risk factor for mortality of stroke [10, 11].

Previous studies had identified anterior wall myocardial infarction as one of the predictors of post-myocardial infarction stroke. Clearly the degree of myocardial damage as measured by the post-myocardial infarction left ventricular ejection fraction (LVEF) was associated with stroke risk. An 18% relative increase in risk for every 5% decrease in LVEF has been demonstrated [8,11]. Other study showed that one-third of patients with ischemic stroke history had more than 50% coronary stenosis [12].

Cardiac injury may cause atrial dysfunction or cardiomyopathy, which signifies an increased risk of Ischemic Stroke even without atrial fibrillation or may cause atrial arrhythmias such as atrial fibrillation, which in turn may lead to an increased risk of ischemic stroke [10]. Ischemic heart disease and myocardial infarction were common cardiac source of embolic stroke, accounting for up  to 30% [13, 14]. Increased coagulation activity during ischemic heart disease, persisting at least up to 6 months, can potentially lead to increased thrombosis and subsequent cardioembolism events [8, 13]. Patients with cardioembolism had a high risk of death and small vessel occlusion have a lower risk of death, which may be associated with cardioembolic occlusion of a large arteries and lack of collateral circulation. Occlusion of a large artery make poor outcome of stroke [11].

In this study risk factor hypertension, dyslipidemia, and atrial fibrillation were more common in the ischemic heart disease group. Modifiable risk factors were the same for both ischemic heart disease and without ischemic heart disease groups, but the risk factors such as hypertension, dyslipidemia, and atrial fibrillation were highly prevalent in ischemic heart disease group. This study was consistent with the results of previous research, cardiovascular disease was a multifactorial disease, stroke patients frequently had comorbidities such as hypertension, diabetes mellitus, heart disease, and dyslipidemia [15-17]. Stroke with various comorbidities such as diabetes mellitus, atrial fibrillation, ischemic heart disease and hypertension will worsen the clinical outcome [18,19].

Atrial fibrillation is present in 7.0% of cases in IHD group. Atrial fibrillation (AF), whether new or chronic, was the single most important risk factor for post-myocardial infarction stroke. Atrial Fibrillation could occur in up to 20% of patients following STEMI and was associated with a significant increase in risk for an in-hospital stroke and increase in-hospital and short-term mortality, increased stroke with profound morbidity [8,13,14].

Hypertension was main vascular risk factor in both groups, but it was more common in IHD group. Hypertension was a known risk factor for cardiovascular disease and blood pressure control was associated with a reduction of recurrent events [20]. Hypertension and dyslipidemia contribute to an increased risk of atherothrombotic stroke [3]. Ischemic heart disease is a marker of severe systemic and cerebrovascular atherosclerotic disease that in turn is associated with Ischemic stroke risk [11]. Previous of severe systemic atherosclerosis such as ischemic heart disease in ischemic stroke was associated with poor outcome of mortality and disability.

Length of stay in ischemic stroke with IHD group was longer than length of stay in ischemic stroke without IHD group (7.50 (0-40) vs 4 (0-14) days). Prolonged hospital stay was associated with the presence of medical complications [21, 22]. Medical complications (gastrointestinal bleeding, decubitus, urinary tract infection and pneumonia) were common in stroke patients with ischemic heart disease (20%). The results of previous studies that complications will increase the risk of death and post stroke complications worsen outcome [23-25].

The limitation of our study was the short-term follow-up. We only observed the in-hospital mortality and in-hospital disability. Further studies should have long-term outcome follow-up to know long-term mortality and disability. Subjects were selected in nonprobability sampling methods with consecutive manner. Using consecutive manner without randomization is a potential source for selection bias. Our study also had several limitations including lack of data on the type of ischemic heart disease, location of ischemic heart disease, echocardiographic findings, and data on medications used. The use of electronic

| Ischemic heart disease | Poor Functional Outcome | Good Functional Outcome | RR (95% Confidence Interval) | p Value |
|------------------------|-------------------------|-------------------------|-----------------------------|---------|
| 60 (60.0%)             | 40 (40.0%)              | 2.6 (1.3 –5.1)          | 0.005                       |
| Mortality              |                         | RR (95% Confidence Interval) | p Value |
| Yes                    | No                      | 2.9 (1.1– 7.3)          | 0.019                       |
| Length of Stay         |                         |                         | 0.001                       |
| 7.50 (0-40) days       |                         |                         |                             |
stroke registry and the fact that the types of variable listed in the electronic stroke registry were relatively complete were the strength of this study.

**Conclusion**

Ischemic stroke patients with ischemic heart disease was associated with higher in-hospital mortality, worse disability, prolonged hospitalization than in ischemic stroke patients without ischemic heart disease.

**Disclosures:** There is no conflict of interest for all authors.

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