

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 a lack. 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

ЖҮРЕКТІҢ ИШЕМИЯЛЫҚ АУРУЫ БАР ЖӘНЕ ЖОҚ НАУҚАСТАРДА ИШЕМИЯЛЫҚ ИНСУЛЬТТИҢ КЛИНИКАЛЫҚ НӘТИЖЕСІН САЛЫСТЫРУ

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ТҰЖЫРЫМДАМА

Мақсаты: Жүректің ишемиялық ауруы және инсульт барлық әлемде аурудың және өлімнің негізгі себептері болып табылады. Ишемиялық инсульт және жүректің ишемиялық ауруы бірдей патофизиологиялық механизмдерге және тәуекел факторларына ие. Жүректің ишемиялық ауруы бар пациенттерде инсульттың жиі пайда болуын аурудың және өлім мәселесімен байланыстырады, дегенмен ишемиялық инсульт кезінде жүректің ишемиялық ауру нәтижесін зерттеу шектеулі. Бұл зерттеу Рэнкиннің (mRS) түрлендірілген шкаласын функционал-

ды нәтижемен қолдану және ұзақ ауруханаға жатқызумен ишемиялық инсульт кезінде жүректің ишемиялық ауруы салыстырылып жатқан алғашқы зерттеу. Бұл зерттеудің мақсаты жүректің ишемиялық ауруымен және олсыз ишемиялық инсультпен пациенттерде клиникалық нәтижені салыстыру болып табылады.

Әдістер: Бетесда Ауруханасының Джокьякарта инсультының Тізімінде (2012-2017) тіркелген алғашқы жіті инсультпен 200 пациентті ретроспективалық топтық зерттеу. Пациенттерді екі топқа бөлген: ишемиялық инсульт және жүректің ишемиялық ауруы бар және жүректің ишемиялық ауруы жоқ ишемиялық инсульты бар пациенттер. Зерттеудің алғашқы нәтижесі аурухана ішіндегі өлім, Рэнкиннің түрлендірілген шкаласы бойынша өлшенетін инвалидизациялау, және ауруханаға жатқызудың ұзақтығы болып табылады. Хи-квадрат және Манна-Уитнидің тестерімен көрсеткіштердің бірфакторлық және бинұсқалық талдамасы өткізілді.

Нәтижелері: Жалпы саны 200 инсультпен және жүректің ишемиялық ауруы бар 100 пациенттен тұрған бірінші топ елу сегіз (58,0%) ерлерді және сексен алты (86,0 %) жастары 50-ден жоғарыларды қамтиды. 100 пациенттен тұратын жүректің ишемиялық ауруы жоқ инсульты бар екінші топ елу сегіз (58,0 %) ерлерді және жастары 50-ден асқан сексен тоғыз (89,0%) пациенттерден тұрады. Инсультпен және жүректің ишемиялық ауруы бар пациенттерден құралған пациенттердің өлімі он сегіз (18%) құрады, алпыс (60%) пациентте жағымсыз функционалды нәтиже (mRS>2) болған және ауруханаға жатқызудың ұзақтығы 10.26±8.39 күн құрады. Бинұсқалық талдама жүректің ишемиялық ауруысыз инсульты бар пациенттер тобына қарағанда инсультпен және жүректің ишемиялық ауруы бар пациенттер тобы аурухана ішіндегі өлімнің жоғары деңгейімен (RR:2.9, 95%CI:1.1–7.3, p<0.019), инвалидизациямен (RR:2.6, 95%CI:1.3 –5.1, p<0.005) және ауруханаға жатқызудың созылуына (10.26±8.39 vs 4.59±2.57, p<0.001) едәуір деңгейде байланысты екенін көрсетті.

Қорытынды: Ишемиялық инсульт және жүректің ишемиялық ауруы бар пациенттер тобы жүректің ишемиялық ауруы жоқ ишемиялық инсульт тобындағы пациенттерге қарағанда үлкен ауруханаға ішіндегі инфекцияларға, нашар инвалидизацияға, ауруханаға жатқызу кезеңінің созылмалдығына байланысты.

Негізгі сөздер: жүректің ишемиялық ауруы, ишемиялық инсульт, салыстыру, клиникалық нәтиже

СРАВНЕНИЕ КЛИНИЧЕСКОГО ИСХОДА ИШЕМИЧЕСКОГО ИНСУЛЬТА У ПАЦИЕНТОВ С И БЕЗ ИШЕМИЧЕСКОЙ БОЛЕЗНЬЮ СЕРДЦА

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РЕЗЮМЕ

Цель: Ишемическая болезнь сердца и инсульт являются основными причинами заболеваемости и смертности по всему миру. Ишемический инсульт и ишемическая болезнь сердца имеют одинаковые патофизиологические механизмы и факторы риска. Частоту возникновения инсульта у пациентов с ишемической болезнью сердца связывают с проблемой заболеваемости и смертности, но изучение ишемической болезни сердца при ишемическом инсульте с исходом ограничено. Настоящее исследование является первым, в котором сопоставляется ишемическая болезнь сердца при ишемическом инсульте с продолжительностью госпитализации и функциональным исходом использования модифицированной шкалы Рэнкина (mRS). Целью настоящего исследования является сравнение клинического исхода у пациентов с ишемическим инсультом с ишемической болезнью сердца и без нее.

Методы: Настоящее ретроспективное когортное исследование 200 пациентов с первым острым ишемическим инсультом, зарегистрированных в Регистре инсульта Джокьякарты Больницы Бетесда (2012-2017). Пациентов разделили на две группы: пациенты с ишемическим инсультом и ишемической болезнью сердца и пациенты с ишемическим инсультом без ишемической болезни сердца. Первичным исходом исследования оказались внутрибольничная смертность, инвалидизация измеряемая по модифицированной шкале Рэнкина, и продолжительность госпитализации. Проводился однофакторный и бивариантный анализ данных с последующими тестами Хи-квадрат и Манна-Уитни.

Результаты: Первая группа из 100 пациентов с инсультом и ишемической болезнью сердца, из общего количества 200, содержит пятьдесят восемь (58.0%) мужчин и восемьдесят шесть (86.0%) пациентов старше 50 лет. Вторая группа из 100 пациентов с инсультом без ишемической болезни сердца содержит пятьдесят восемь (58.0%) мужчин и восемьдесят девять (89.0%) пациентов старше 50 лет. Смертность пациентов группы с инсультом и ишемической болезнью сердца составила восемнадцать пациентов (18.0%), у шестидесяти пациентов (60%) был неблагоприятный функциональный исход (mRS >2) и продолжительность госпитализации составила 10.26 ± 8.39 дней. Бивариантный анализ показал, что группа пациентов с инсультом и ишемической болезнью сердца в значительной степени связана с высоким уровнем внутрибольничной смертности (RR:2.9, 95%CI:1.1–7.3, p<0.019), инвалидизацией (RR:2.6, 95%CI:1.3 –5.1, p<0.005) и затянувшимся периодом госпитализации (10.26±8.39 vs 4.59±2.57, p<0.001), чем в группе пациентов с инсультом без ишемической болезни сердца.

Заключение: Группа пациентов с ишемическим инсультом и ишемической болезнью сердца в значительной степени связаны с большей внутрибольничной инфекцией, худшей инвалидизацией, затянувшимся периодом госпитализации, чем в группе пациентов с ишемическим инсультом без ишемической болезни сердца.

Ключевые слова: ишемическая болезнь сердца, ишемический инсульт, сравнение, клинический исход

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 had been followed up from the first day until they were died in-hospital or discharge from the hospital.

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.

Ethic

This study used secondary data. Research Ethics Committee of Duta Wacana Christian University School of Medicine had approved the study. Ethical clearance for conducting the study was obtained from the ethic committee, Duta Wacana Christian University School of Medicine Yogyakarta, Indonesia.

Statistical Analysis

The statistical analysis was performed by licensed SPSS version 23,0. We considered that significance level is $P < 0.05$. The data analyzed with Chi-square test was used for categorical variable and Mann-Whitney for continuous. Categorical data presented as percentages and continuous data presented as median and minimum-maximum if abnormally distributed. We used RR (Related Risk) and 95% Confidence Interval to show the comparison.

Results

From January 2012 to December 2017, there were 6526 subjects who had suffered from ischemic stroke and 1685 had incomplete data and were excluded from this study. Subjects were selected in consecutive manner until required subject obtained. Table 1 showed the subjects characteristics of the remaining 200 subjects. The data obtained from 200 patients consisted of 100 ischemic stroke patients with history of ischemic heart disease and 100 ischemic stroke patients without history of ischemic heart disease. The subjects were predominantly males. Older age (age more than 50 years old) were more common in IHD group. The most subjects in IHD group came to hospital more than 6 hours (54.0%) after stroke onset. Almost half (42.0%) of the patients with history of IHD group had dyslipidemia and hypertension was present in 52.0% of cases. Atrial Fibrillation (7 %) and Complication (20%) were more often in ischemic stroke patients with ischemic heart disease. Late onset was more frequently in patients without IHD group (64.0%). Complication in patients without IHD consist of four patients (4%). The most prominent risk factor of the patients without IHD group was hypertension (49%).

Table 1 Characteristics of patients with ischemic heart disease compared to patients without ischemic heart disease

	Ischemic Heart Disease	No Ischemic Heart Disease	p-value
	N	n	
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.

Table 2

Association of ischemic heart disease with clinical outcomes.

Ischemic heart disease	Disability		RR (95% Confidence Interval)	p Value
	Poor Functional Outcome	Good Functional Outcome		
	60 (60.0%)	40 (40.0%)	2.6 (1.3 – 5.1)	0,005
	Mortality		RR (95% Confidence Interval)	p Value
	Yes	No		
	18(18.0%)	82(82.0%)	2.9 (1.1– 7.3)	0,019
	Length of Stay		p Value	
	7.50 (0-40) days		0,001	

Discussion

The main purpose of this study was to compare clinical outcomes of ischemic stroke patients with ischemic heart disease and without ischemic heart disease. The present study there was association between ischemic heart disease in ischemic stroke with mortality, disability and length of stay in hospital. Ischemic stroke patients with ischemic heart disease was associated with twofold higher mortality and with threefold higher poor functional outcome in acute ischemic stroke patients.

Similarly, in previous study ischemic stroke patients following an ischemic heart disease had increased in-hospital and long-term mortality with in-hospital mortality of 30%, more acute and more extensive deficits, and greater residual deficits at 6 months [8]. 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

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.

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

Conclusion

Ischemic stroke patients with ischemic heart disease was

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

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