In Hospital Atrial Fibrillation is a Predictor of Long Term Stroke Event among Patients with Acute Myocardial Infarction

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Background. Atrial fibrillation (AF) is a common arrhythmia after acute myocardial infarction (AMI).Mortality in AMI patients with AF also been shown to be up to twice as high as for those without AF. Nonhemorrhagic stroke occurs in 0.1% to 1.3%of patients with acute myocardial infarction who are treatedwith thrombolytic, with substantial associated mortality andmorbidity. The aim of this study is toelaborate correlation between in hospital AF with long term stroke event inST-elevation myocardial infarction (STEMI) patients who treated with thrombolytic .

Methods. Two hundred and thirty STEMI patients (27-72 yo) treated with thrombolytic agent were studied retrospectively. The study end point was Major Cardio-Cerebrovascular Event (MACCE) during 3 years follow up.

Results. Eleven patients experience AF episode during STEMI hospitalization. During 3 years follow up 24 patients (10.4%) experienced MACCE which comprised of : cardiac death 4 (1.7%), fatal infarction 2 (0.9%), non fatal infarction 13 (5.7%) and stroke 5 (2.2%). Independent clinical variables were not significant as a predictor for the occurrence of future stroke event, except atrial fibrillation episode (HR 13.4; p<0.005) that was encountered during hospitalization in the setting of AMI.

Conclusion. In-hospital AF in STEMI patients treated with thrombolytic agent is a predictor of long term stroke.

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Keywords: Acute Myocardial Infarction, Stroke, Atrial Fibrillation

Fibrilasi Atrial Selama Perawatan Infark Miokard Akut Merupakan Prediktor Stroke Jangka Panjang

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Latar belakang. Fibrilasi atrium (AF) merupakan aritmia yang sering terjadi setelah infarct miokard akut (IMA). Mortalitas pada pasien IMA dengan AF meningkat dua kali lipat. Stroke non hemoragik terjadi pada 0.1 hingga 1.3% pasien IMA yang mendapat trombolitik. Tujuan penelitian ini untuk melihat korelasi antara AF selama perawatan IMA Elevasi Segmen ST (IMAEST) dengan kejadian stroke.

Metoda. Studi kohort retrospektif terhadap 230 pasien IMAEST yang mendapat terapi trombolitik. Kejadian serebro-kardiovaskular mayor (KSKM) dicatat dalam masa pengamatan 3 tahun.

Hasil. Sebelas pasien mengalami AF dalam perawatan. Dua puluh empat (10.4%) pasien mengalami KSKM yaitu kematian jantung 4 (1.7%), infark yang fatal 2 (0.9%), infark non fatal 13 (5.7%) dan stroke 5 (2.2%). AF merupakan faktor risiko independenuntuk kejadian stroke (HR 13.4, p < 0.005).

Kesimpulan. AF selama perawatan IMA yang mendapat trombolitik merupakan prediktor stroke jangka panjang.

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Kata kunci: Infark miokard akut, stroke, fibrilasi atrial

Atrial fibrillation (AF) is the common sustained arrhythmia in the general population with about 1-2% prevalence and 0.1-0.2% annual incidence. The frequency of AF increases markedly with age and in octogenarians.[1, 2]The annual prevalence and incidence of AF are reported to be greater than 6 and 2% respectively. As AF leads to the formation of thrombus in the left atrium, especially its appendage, individuals with AF have significant sixfold increase in their risk of ischaemic stroke and systemic cardioembolism when compared with those subjects with normal sinus rhythm.AF increases incidence of stroke independently of other important vascular risk factor such as hypertension, hyperlipidemia, and diabetes mellitus. AF is a common arrhythmia after acute myocardial infarction (MI), with reported incidence in previous studies between 5% and 23%. Atrial Fibrillation may have been pre-existing before acute MI or developed acutely following acute MI due to ischemia of the sinus node or atrial myocardium, or sub acutely following the development of congestive heart failure or pericarditis. Mortality in acute MI

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patients with AF also been shown to be up to twice as high as for those without AF.

Stroke is one of the most feared complications in patients withacute myocardial infarction. In the era before the routine useof thrombolytic therapy and anticoagulation, stroke was observedin 1.7% to 3.2% of patients. Intracranial hemorrhagewas exceedingly rare. In the thrombolytic era, the overall incidenceof stroke in large clinical trials is lower, but the types of strokeshave changed. Nonhemorrhagic stroke now occurs in 0.1% to 1.3% of patients, and intracranial hemorrhage occurs in 0.07% to1.5% of patientswho are treatedwith thrombolytic, with substantial associated mortality andmorbidity. However, the mechanisms behind strokes related MIare not clear.[3-6]

Less is known about the risk factors for non-hemorrhagicstroke in patients with acute myocardial infarction treated with thrombolytic therapy,[7] although several investigators have reported clinical and echocardiographic factors associated withan increased risk for non-hemorrhagic stroke.[8]

The aim of this study is to examine the incidenceof Major Cardio-Cerebrovascular Event (MACCE) during 3 years after an acute myocardial infarction in patients who treated with thrombolytic therapy and to identify the predictors of myocardial infarction related stroke.

Methods

This is a retrospective cohort longitudinal study. Patients were enrolled based on registry of acute myocardial infarction at the National Cardiovascular Center Harapan Kita (NCCHK) hospital, during the period of January 1997 until June 1999 and were observed and followed up until January 2000.

The criteria for the diagnosis of acute MI were standardized and were identical for all participating hospital using the World Health Organization (WHO) criteria. A diagnosis of myocardial infarction was based on typical chest pain, electrocardiographic findings and a diagnostic elevation of cardiac enzymes. Two of three criteria were required.

All the participants were received thrombolytic therapy.

In brief, patients presenting with acute myocardial-infarction within 12 hours of symptom onset were given intravenous 1.5 million units streptokinase over 1 hour and continue with intravenous heparin or unfractionated heparin for 5 days. All patients received aspirin (80-160 mg) daily.

The WHO definition of stroke was used: rapidly developing clinical sign of focal (or global) disturbance of cerebral function lasting more than 24 hours (unless interrupted by surgery or death) with no apparent cause other than a vascular origin.

All clinical variables were recorded from medical record file, such as age, sex, risk factors, laboratory data, electrocardiography (ECG) recording and other variables during hospitalization such as drug treatment of the acute MI, progression of angina, recurrent infarction, arrhythmias, and heart failure. After discharged the patients were monitored and followed up for the end points of cardiac related death, fatal and non-fatal MI, and fatal and non-fatal stroke. All clinical variables and hospitalization variables were tested to dependent variable stroke event.

Statistical analysis

Group data are expressed as mean ± standarddeviation (SD) for continuous variable and as count (percentage) for nominal variable. Differences between proportions were analyzed withnon-parametric test. The risk of MI-related stroke associated with different clinical characteristics is given by Odds Ratio (OR) with confidence interval (CI) 95%. Variable associated with a risk for MI-related stroke in univariate analysis or considered to be of potential clinical interest were included in the model. Kaplan Meir survival curves were calculated for patients with and without MI-related stroke and compared between groups with the log rank test. The Cox proportional hazards model was used to identify predictors of stroke event. Data were analyzed with SPSS version 11.5. The p value of<0.05 considered as statistically significant.

Results

During period of January 1997 up to June 1999, 230 Acute ST elevation Myocardial Infarction patients aged 27-72 yearstreated with thrombolytic therapy were included in this study. Mean follow up time was 33.67 ± 7.8 months (range of 1-42 months). Six subjects (2.6%) were lost tofollow up. Atrial fibrillation was occurred in 11 (4.78%) patients. Clinical characteristics and clinical finding during

Table 1. Baseline characteristic of study population

Variable		AF (n=11)	Non AF (n=219)	p
Age	< 45	3 (27.27)	51 (23.29)	NS
	> 45	8(72.73)	168(76.71)	
Sex	Male	10(90.91)	204(93.15)	NS
	Female	1(9.09)	15(6.85)	
Diabetic	Yes	0 (0)	43 (19.63)	NS
	No	11(100)	176(80.36)	
Hypertension	Yes	6 (54.55)	79(36.07)	NS
	No	5 (45.45)	140(63.92)	
Previous AMI	Yes	1 (9.09)	27(12.33)	NS
	No	10 (90.91)	192(87.67)	
Previous Angina	Yes	3(27.27)	59(26.94)	NS
	No	8(72.73)	160(73.06)	
Conduction disturbance	Yes	5 (45.45)	27(12.33)	NS
	No	6 (54.55)	192(87.67)	
Heart Failure	Yes	2 (18.18)	34(15.53)	NS
	No	9 (81.82)	185(84.47)	
In hospital reinfarction	Yes	0 (0)	2(0.91)	NS
	No	11(100)	217(99.09)	

Data were presented as count (percentage)

the hospital stay of the two groups are compared in table 1. There were no significant differences between two groups in term of baseline characteristics of study population.

Total MACCE during follow up period was 24 patients (10.4%). Four patients (1.7%) were dead including 2 patients (0.9%) with fatal infarction; 13 patients (5.7%) had non-fatal MI, and stroke was occurred in 5 patients (2.2%). Stroke event ratewas 18.18% in AF group and 1.37% in Non AF group (p<0.001) (figure 1). Annual stroke event rate in AF group was 4 %.

Table 2. Univariate Analysis

Variable	OR (CI 95%)	p
AF	1.2 (1.10-1.6)	0.01*
> 45 yo	1.02 (0.9-1.06)	0.25
Female	3.06 (0.49-18.51)	0.30
Non Diabetic	1.23 (0.63-1.32)	0.35
Hypertension	1.08(0.36-3.22)	0.61
Previous AMI	1.67(0.28-9.97)	0.48
Previous Angina	1.09 (0.70-1.71)	0.59
Non Conduction disturbance	1.16 (0.49-1.23)	0.47
Heart Failure	2.65 (0.87-8.09)	0.27
Non in hospitality reinfarction	1.01 (0.98-1.02)	0.96

Table 3. Multivariate analysis

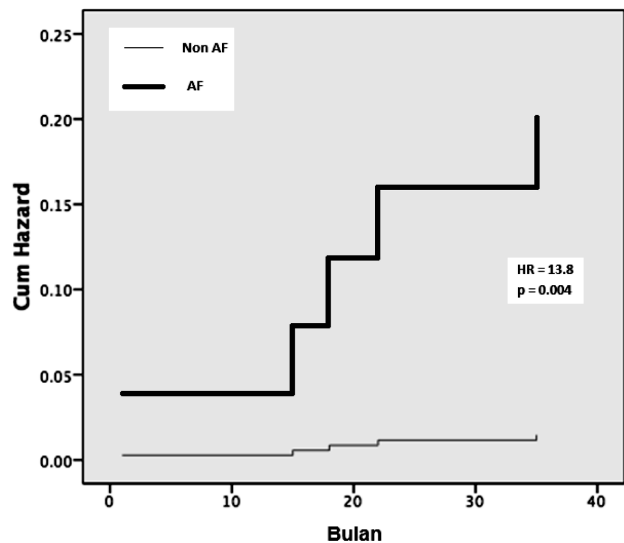| Variable	HR (CI 95%)	p
AF	13.8 (2.3-82.4)	0.004*
Age > 45 yo	1.01 (0.92-1.11)	NS
Female	0.34 (0.03-3.0)	NS

Figure1. Cummulative hazard of stroke event among post-acute MI patients treated with thrombolytic therapy.

Univariate and multivariate analysis (table 2 and table 3) showed that the occurrence of AF during hospitalization significantly increase the risk of stroke event with HR 13.8 (CI 95% 2.3-82.4).AF was identified as independent predictors of stroke event in the present study.

Discussion

This study find that in-hospital AF of acute MI patient is an independent predictor of non-hemorragic stroke during mean follow-up of 33 months.

This finding supports previous findings that showed patients with AF also had a higher likelihood of non-hemorrhagic strokethan patients who never experiencedAF/atrial flutter duringthe hospital stay.

Stroke after an acute MI is an infrequent but important clinical problem. The incidence of MI-related stroke has been estimated in several studies both before and after introduction of aspirin and thrombolytic as standard therapy. Previous study found that stroke event rate after an acute MI that treated with thrombolytic therapy was 2.2%.[3]

This study revealed relatively low incidence of AF (4.78%) in acute MI patients. The incidence of AF in patients with acute MIvary depending on the population sampled. In the Cooperative Cardiovascular Project, 22% of Medicare beneficiaries65 y or older hospitalized for acute MI had AF.[9] Lower rates of AF were observed in patients selected for other prospective trials, such as the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO-I) study, in which the incidence was 10.4%,[10] but this may reflect the youngerage of patients presenting with acute MI associated with ST-segment elevation on the ECG. In our study most of subject aged less than 60 years old which support the previous study. AF is more commonly associated with acute MI in older patients and those withhigher Killip class or LV dysfunction. AF is associated with increased in-hospital mortality in thesetting of acute MI (25.3% with AF vs. 16.0% without AF),30-d mortality (29.3% vs. 19.1%), and 1-y mortality (48.3%vs. 32.7%).[9] Patients who developed AF during hospitalizationhad a worse prognosis than those with AF onadmission.[9] Stroke rates are also increased in patientswith MI and AF compared with those without AF.[10]

The present study has several limitations. All the AF patients were pooled together as a single category without classification of paroxysmal, persistent, or permanent AF. The mechanism of non-hemorrhagic stroke was not determined, and some strokes may not have been related to cardiac events or procedures. Because of echocardiography was not mandated by this study protocol, the incidence of left ventricular thrombusin this study is unknown. Finally, these results are only applicable to the patients with acute myocardial infarction treated with thrombolytic therapy and should not be generalized to all patients with acute myocardial infarction.

Conclusion

AF episode during hospitalization in patients with acute MI is strongly related to the occurrence of stroke. This finding emphasis that AF should be recorded and taken into account as a marker of poor prognosis. Further study to seek efficacy of medical intervention with anti-arrhythmic drugs and/or anticoagulant/antiplatelet therapy as a secondary prevention of stroke event in the future.

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