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Original Article

Prognostic impact of atrial fibrillation in patients with acute myocardial infarction

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ABSTRACT

Background: Atrial fibrillation (AF) is the most common supraventricular tachyarrhythmia in patients with acute myocardial infarction (AMI). However, little is known about the impact of AF on in-hospital and long-term mortalities in patients with AMI in the era of primary percutaneous coronary intervention (PCI).

Methods: Six hundred ninety-four consecutive patients with AMI admitted within 48 h after symptom onset were analyzed. All patients successfully underwent primary PCI at the acute phase of AMI. Patients were divided into 2 groups according to the presence of AF at admission or during index hospitalization. We retrospectively evaluated the in-hospital and long-term all-cause mortalities between patients with and those without AF.

Results: AF was detected in 38 patients (5.5%) at admission and in 51 patients (7.3%) during hospitalization. Patients with AF were older and had a higher heart rate, lower ejection fraction, higher prevalence of hypertension, worse renal function, higher peak level of creatine phosphokinase, and lower rate of final TIMI flow grade 3 than those without AF. Although patients with AF had a more complicated clinical course and higher in-hospital mortality (11.2% vs. 4.0%, $P=0.009$), there was no significant association between presenting AF and in-hospital death after adjustment for baseline confounders (odds ratio, 2.63; 95% confidence interval [CI], 0.91–5.47; $P=0.076$). During the follow-up period of 3.0 ± 1.7 years, patients with AF had a higher all-cause mortality than those without AF (30.3% vs. 22.1%, $P=0.004$ by log-rank test). However, after adjustment for clinical characteristics, presenting AF was not an independent predictor of all-cause mortality (hazard ratio, 1.15; 95% CI, 0.67–1.88; $P=0.588$).

Conclusions: AF is a common complication of AMI and associated with a more complicated clinical course. However, AF is not an independent predictor of both in-hospital and long-term mortalities in the PCI era.

1. Introduction

Atrial fibrillation (AF) is the most common supraventricular tachyarrhythmia seen in patients with acute myocardial infarction (AMI). It has been reported that AF occurs in 5–23% of patients with AMI [1–4]. AF is triggered by many different conditions, including left ventricular dysfunction with hemodynamic impairment [5,6], atrial ischemia or infarction [7], pericarditis, chronic lung disease, acute hypoxia, or electrolyte abnormalities [8,9]. AF occurring during the acute phase of AMI may adversely affect the left ventricular function and exacerbate ongoing myocardial ischemia. The bidirectional interaction between AF and myocardial dysfunction or ischemia may lead to a vicious circle in a patient with AF complicating AMI. Some studies have shown an association between increased in-hospital and long-term mortalities and AF [1,10–13], although others have found no independent effect [2,3,14–17]. Most studies on AF complicated with AMI were performed in the prethrombolytic or thrombolytic era. Current treatments for AMI include not only aspirin, β-blockers, and thrombolytic therapy, but also angiotensin-converting enzyme inhibitors (ACE-I), angiotensin II receptor blockers (ARB), statin, and percutaneous coronary intervention (PCI) [18]. PCI has been shown to be a more effective treatment strategy in patients with AMI than thrombolytic therapy [19,20], and use of primary PCI has dramatically increased [21]. However, little is known about the in-hospital and long-term mortalities in patients with AMI and AF in the PCI era. We examined the impact of AF on in-hospital and long-term mortalities in patients with AMI.

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2. Methods

2.1. Study patients

The study protocol was approved by the ethical committee on human research of our institution. Six hundred ninety-four consecutive AMI patients who were transferred to Hirosaki University Hospital within 48 h after symptom onset and underwent primary PCI at the acute phase of AMI from February 2006 to April 2010 were enrolled. The diagnosis of AMI was made in the presence of chest pain lasting $\geq$20 min and/or electrocardiographic (ECG) changes suggestive of myocardial infarction (MI) or ischemia ($\geq$0.1 mV ST-segment elevation or depression in $\geq$2 contiguous leads and/or appearance of a new Q-wave), accompanied by an increase of creatine phosphokinase myocardial isoform (CPK-MB) and/or a cardiac troponin T-value greater than the upper reference limit. AF was defined electrocardiographically as the absence of P-waves, coarse or fine fibrillation waves, and completely irregular R-R interval, and was diagnosed by 12-lead ECG or ECG monitoring by at least 2 cardiologists.

The study population was divided into 2 groups: patients who had AF at admission or developed AF during hospitalization (any-AF group) and those without AF (non-AF group). The any-AF group was further divided into 2 subgroups: patients who had AF at admission (AF at admission) and those who did not have AF at admission but developed AF during the index hospitalization (AF during hospitalization). Patients with a history of paroxysmal or transient AF but without a recurrence of AF during the index hospitalization were categorized into the non-AF group.

2.2. Primary PCI

Primary PCI was performed in accordance with the ACC/AHA/SCAI Practice Guidelines for Percutaneous Coronary Intervention [22]. Patients admitted within 12 h of symptom onset were indicated for primary PCI. Those admitted within 36 h of AMI onset and complicated with cardiogenic shock, or those admitted after 12 h but within 24 h and complicated with severe heart failure, hemodynamic or electrical instability, or evidence of persistent ischemia also underwent primary PCI. Patients who were admitted >12 h after AMI onset and were hemodynamically and electrically stable were not submitted to primary PCI. A bare metal stent was used for PCI when stenting was indicated.

2.3. Endpoints

The primary endpoint of the study was all-cause death. We retrospectively evaluated the in-hospital and long-term all-cause mortalities. We also examined the association of AF with in-hospital events, including congestive heart failure (CHF), cardiogenic shock, ventricular tachycardia/fibrillation (VT/VF), stroke, and length of hospitalization. Follow-up started from the day of admission. The patients were followed for 3.0 $\pm$ 1.7 years. After hospital discharge, follow-up data were obtained from the following 3 ways: reviewing patients' hospital records, interviewing the patients through telephone, and examining the patients in outpatient clinics.

2.4. Statistical analysis

Continuous parameters were expressed as mean $\pm$ SD, and categorical variables as number and percentage. Comparative analysis among groups was performed with Student's *t* test or ANOVA for continuous variables and chi-square test for categorical variables. For comparison of non-AF, AF at admission, and AF during hospitalization, Tukey's honest significant difference test multiple-comparison procedure was used to identify where the differences among the 3 groups occurred after the significant ANOVA. A multivariate logistic regression model was used to analyze factors that influenced the prevalence of AF. The following variables were entered into the model: age >65 years, male sex, heart rate at admission >100/min, left ventricular ejection fraction (LVEF) <40%, anterior MI, peak level of CPK >3000 IU/L, final TIMI flow grade 3, and Killip class at admission >I. The prognostic impact of AF on in-hospital mortality was examined using a multivariate logistic regression model, adjusting for age >65 years, LVEF <40%, and final TIMI flow grade 3. Kaplan–Meier curves for long-term all-cause mortality among the groups were constructed and compared using the log-rank test. Univariate and multivariate Cox proportional hazard analyses were performed to identify hazard ratios (HR) and 95% confidence intervals (CI). All AF categories (any-AF, AF at admission, and AF during hospitalization) were tested in a univariate model and furthermore in a multivariate model adjusted for clinical prognostic factors, including age >65 years, male sex, LVEF <40%, estimated glomerular filtration rate (eGFR) <60 mL min^{-1} 1.73 m^{-2}, anterior MI, peak level of CPK >3000 IU/L, heart rate at admission >100/min, and final TIMI flow grade 3. All statistical analyses were done using JMP 10.0.2 (SAS Institute Inc., Cary, NC, USA). A *P* value of <0.05 was considered significant.

3. Results

3.1. Baseline characteristics and relation to AF

The baseline characteristics of the patients are summarized in Table 1. Of the 694 patients, AF was diagnosed in 89 (12.8%, any-AF group) at admission (38 patients, 5.5%) or during hospitalization (51 patients, 7.3%). Of the 89 patients with AF, AF was terminated spontaneously in 31 (34.8%), by electrical cardioversion in 17 (19.1%), with intravenous or oral administration of amiodarone in 29 (32.6%), with intravenous β-blocker in 7 (10.8%), and was not terminated during index hospitalization in 23 (25.8%). Patients with any-AF were older and had a higher heart rate, lower LVEF, lower eGFR, higher prevalence of hypertension, higher peak level of CPK, lower rate of final TIMI flow grade 3, and higher prevalence of previous AF than those without AF. Particularly, patients with AF at admission had a significantly higher heart rate at admission and a higher prevalence of previous AF. Patients with AF during hospitalization had a higher prevalence of hypertension than those without AF. No significant difference was found in sex, body mass index, left atrial dimension, diabetes mellitus, anterior MI, time from symptom onset to presentation, Killip class at admission, history of MI, stroke, and previous PCI. Multivariate logistic regression analysis revealed that age >65 years, male sex, heart rate >100/min, and peak level of CPK >3000 IU/L were independent predictive factors of the prevalence of AF (Table 2).

The medication at discharge is shown in Table 3. Patients with AF were more commonly treated with warfarin and β-blockers, but were less administered thienopyridine. There were no significant difference in the treatments with ACE-I, ARB, and statin between the non-AF and any-AF groups. Eighty-four patients (12.7%) were treated with aspirin, thienopyridine, and warfarin (triple antithrombotic therapy). Triple antithrombotic therapy was more frequently administered in patients with AF than in those without AF. Neither use of warfarin nor use of antiplatelet drugs had a significant relation to long-term mortality.

3.2. Impact of AF on in-hospital events

CHF, cardiogenic shock, and VT/VF occurred more often in patients in the any-AF group than in those in the non-AF group, and hospitalization was also longer in patients with than in those without AF. There was no significant difference in the incidence of in-hospital stroke (Table 4). Of the 34 patients (4.9%) who died