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Original Contribution

Coronary atherosclerosis and adverse outcomes in patients with recent-onset atrial fibrillation and troponin rise☆

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ABSTRACT

Background: The relationship between troponin and atrial fibrillation (AF) without acute coronary syndrome is still unclear. We sought to investigate the presence of coronary atherosclerosis and adverse outcomes in patients with AF.

Methods: Consecutive patients with recent-onset AF and without severe comorbidities were enrolled between 2004 and 2013. Patients with a troponin rise or with adverse outcomes were considered for coronary angiography and revascularization when "critical" stenosis (≥70%) was recognized. Propensity score matching was performed to adjust for baseline characteristics; after matching, no differences existed between the groups of patients with or without troponin rise. The primary end point was the composite of acute coronary syndrome, revascularization, and cardiac death at 1- and 12-month follow-ups.

Results: Of 3627 patients enrolled, 3541 completed the study; 202 (6%) showed troponin rise; and 91 (3%), an adverse outcome. In the entire cohort, on multivariate analysis, the odds ratio for the occurrence of the primary end point of troponin rise was 14 (95% confidence interval [CI], 10-23; $P < .001$), and that of known coronary artery disease was 3 (CI, 2-5; $P = .001$). In the matching cohort, the odds ratio of troponin rise was 10 (CI, 4-22; $P < .001$), and that of TIMI score greater than 2 was 4 (CI, 2-9; $P \leq .001$). In the entire cohort, patients with or without troponin rise achieved the primary end point in 38 (19%) and 43 (1%) patients, respectively ($P < .001$). Stroke occurred in 4 (2%) and 20 (1%), respectively ($P = .018$). Critical stenosis and revascularization account for 23 (12%) and 15 (1%), respectively ($P < .001$). In the matching cohort, results were confirmed, but incidence of stroke was comparable.

Conclusions: Patients with recent-onset AF and troponin rise showed higher prevalence of coronary atherosclerosis and adverse cardiac events. Stroke per se did not succeed in justifying the high morbidity. Thus, beyond stroke, coronary atherosclerosis might have a pivotal role in poor outcomes.

1. Introduction

In recent times, atrial fibrillation (AF) has reached a high prevalence in the general population especially in patients with hypertension, coronary artery disease (CAD), cardiomyopathy, and diabetes mellitus [1-3] and represents the most common cardiac arrhythmia encountered in acute cardiac care [1,4]. Atrial fibrillation is associated with a reduction in the quality of life and with increased risk of stroke, heart failure, and mortality [1,3,5,6]. Present-day clinical efforts should focus on the prevention of complications associated with AF and treatment of comorbidities that contribute to excess mortality, especially with secondary prevention strategies, in patients with hypertension, heart failure, and coronary atherosclerosis [7-11].

Several studies associate AF with the presence of CAD, troponin elevations, and adverse cardiac events [12-14]. Troponin, a marker of myocardial injury, plays a role in the risk assessment of patients with CAD, and patients with elevated levels of troponin are at increased risk for cardiac events [4,15]. However, it is unclear whether elevated levels of cardiac troponin, in patients with AF without acute coronary syndrome (ACS), could indicate the presence of coronary atherosclerosis. Indeed, myocardial infarction is an established risk factor for AF, with AF occurring up to 20% of patients with myocardial infarction, and the presence of AF during acute myocardial infarction has been associated with an increased risk of developing inhospital reinfarction [16,17].

☆ The authors declare no potential conflicts of interest.

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These findings suggest that AF could also be a risk factor for coronary events [18]. Unfortunately, strong evidence to support this suggestion is lacking [12,19,20].

The purpose of this study was to investigate the relationship of coronary atherosclerosis and adverse outcome with troponin rise and recent-onset AF.

2. Patients and methods

2.1. Study population

Patients were enrolled between January 2004 and December 2013 at the emergency and cardiology departments of the tertiary care teaching Careggi Hospital in Florence, Italy. The inclusion criterion was the presence of recent-onset AF (ie, AF lasting <48 hours) confirmed by electrocardiogram (ECG) on presentation. The exclusion criteria were the presence of ACS or stroke, Killip class greater than or equal to 2, and hemodynamic instability. In addition, patients with severe renal disease and severe chronic obstructive pulmonary disease were excluded [4,15,21]. Patients were followed up through December 2014.

Each patient gave informed consent to participate in the study and for publication of personal data. The study was conducted in accordance with Good Clinical Practice guidelines and principles of the Declaration of Helsinki. The institutional review board approved the protocol. Departmental sources supported the work, and no contributorship or competing interest existed.

2.2. Management of patients and data collection

Duration of AF was self-reported or determined according to the clinical history. All the patients underwent ECG, clinical evaluation, and serial blood tests, including troponin plasma levels, on presentation. Patients were most likely to submit to observation, echocardiography, and stress testing or discharged based on clinical evolution. The therapeutic approach and disposition were at the discretion of the physician on duty, especially before the general consensus that occurred in the last months of 2012, on the high risk for cardiac events in patients with a recent onset of AF and troponin rise [14,22].

All the patients with troponin rise were considered for angiography, whereas patients without troponin rise were considered for angiography or noninvasive angiography by multislice computed tomography when they presented adverse coronary events on the follow-up period or if they were demonstrated as having abnormal echocardiography or abnormal stress testing, during inhospital or outpatient evaluation, or if they presented a very high-risk clinical profile, at least.

The subset of patients who underwent coronary angiography, within 1 month from the onset of AF, were stratified by the presence of troponin rise. A quantitative evaluation of lesions in the coronary tree was compared. “Critical” coronary stenosis was considered in the presence of stenosis greater than or equal to 70%; “moderate-subcritical” coronary stenosis, in the presence of stenosis greater than or equal to 50% to 69%; and “mild-subcritical”, greater than or equal to 30% to 49%. Patients with stenosis less than 30% were considered free of obstructive coronary artery disease.

2.3. Definition of covariates

Data on risk factors for atherosclerosis, comorbidities, and pharmacological treatment were self-reported and confirmed after reviewing the clinical charts; congestive heart failure history = 1 point, hypertension history= 1 point, age greater or equal to 75 years = 1 point, diabetes mellitus history = 1 point, stroke or transitory ischemic attack symptoms previously = 2 points ($CHADS_2$) score and thrombolysis in myocardial infarction (TIMI) risk score were calculated. After discharge, patients with a $CHADS_2$ score greater than or equal to 1 were recommended for oral anticoagulant therapy [23-25]. Known existing coronary, carotid, and peripheral artery diseases referred to the presence of lesions greater than or equal to 50% in any vessel [26]. Diabetes mellitus and hypertension were diagnosed according to guidelines [27,28]. Hemodynamic instability was defined by the presence of systolic blood pressure less than or equal to 100 mm Hg [29]; moderate to severe renal disease was indicated by plasma creatinine levels greater than or equal to 2.3 mg/mL or a calculated glomerular filtration rate less than 30 mL/min by Modification of Diet in Renal Disease [30]. The diagnosis of ACS was considered in the presence of a ST-segment depression greater than or equal to 0.1 mV or ST-segment elevation greater than or equal to 0.1 mV in 2 contiguous electrocardiographic leads, at least, measured at 60 milliseconds from J point, according to the European and North American guidelines [31,21].

2.4. Troponin assay

Serial blood samples were obtained from all patients on admission and eventually up to 6 to 12 hours based on clinical evolution. Samples were submitted to our core laboratory for analysis, carried out using the high-sensitivity plasma concentration of troponin I assay ADVIA Centaur TnI-Ultra (Siemens, Erlangen, Germany). The cutoff value for plasma concentration of troponin I levels in our laboratory was 0.10 ng/mL or higher as the 99th percentile of a control group [15,32].

2.5. End point

The primary end point was the composite of ACS, revascularization, and cardiac death at the 1- and 12-month follow-ups. The secondary end point was the incidence of critical or subcritical coronary stenosis and the occurrence of ischemic stroke.

2.6. Follow-up

Follow-up was performed until December 2014 at 1 month, 1 year, and 10 years by reviewing the emergency department admission archives and over the telephone. Each cardiovascular event was analyzed and confirmed after reviewing clinical charts, ECG results, and laboratory tests.

2.7. Statistical analysis

Summary data are expressed as absolute numbers and percentage for categorical variables and mean ± SD for continuous values. Statistical comparisons of demographics and clinical features were performed using the χ^2 and Pearson exact tests for categorical variables, whereas the Student t test was used for continuous variables (Wilcoxon rank sum test). $P < .05$, from a 2-sided test, was considered to indicate statistical significance. Kaplan-Meier methods were used to estimate event rates at 1-month, 1-year, and 10-year follow-ups in patients with or without troponin rise and to plot time-to-event curves; comparisons were made using the log-rank test or the stratified log-rank test in the propensity score–matched cohort. Because there were significant differences in baseline characteristics between patients with vs without troponin rise, propensity score matching was used to adjust for possible confounders [33]. SPSS software allows estimation of the propensity score using logistic regression and specifying nearest-neighbor matching. Detailed balance statistics and graphs are produced by the program. A 5:1 matched analysis based on the propensity score of each patient was conducted. To ensure good matches, a caliper (maximum allowable difference between 2 participants) of 0.15 was defined. Variables included in the model were age, sex, hypertension, hypercholesterolemia, diabetes mellitus, active smoking, known coronary heart disease, known peripheral vascular disease, prior stroke/transient ischemic attack, cardiomyopathy, chronic renal disease, heart rate, systolic arterial pressure, TIMI risk score, and $CHADS_2$ score. Cox analysis regression model was performed to identify independent predictors for primary end point.

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