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Long-term mortality of patients with atrial fibrillation undergoing percutaneous coronary intervention with stent implantation for acute and stable coronary artery disease

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ABSTRACT

Background: Patients with atrial fibrillation (AF) are of increased risk for ischemic and bleeding complications, particularly when requiring aggressive antithrombotic therapy after coronary stenting. However, data from unselected patients on long-term mortality are scarce.
Methods: We analyzed 2890 patients of a single-center registry undergoing coronary stenting between 2003 and 2012, of whom 1434 patients had stable coronary artery disease (CAD), while 1456 patients presented with acute coronary syndromes (ACS). As the primary endpoint, we compared long-term all-cause mortality between patients with AF and patients in sinus rhythm.
Results: History or presence of AF was found in 146 (10.2%) patients with stable CAD and 93 (6.4%) patients with ACS. The median CHA_2DS_2-VASc scores were similar between stable CAD and ACS patients (4[2; 5] vs. 3[2; 5], $p = 0.92$). Patients with AF had a significantly higher atherothrombotic risk profile and more co-morbidities. Patients undergoing PCI before 2011 received triple therapy (aspirin, clopidogrel and a vitamin K antagonist) in 25% of cases, compared to 64% of cases thereafter.
Patients undergoing elective or urgent revascularization and suffering from AF had a similar 2-fold increased adjusted relative risk of death after a mean follow-up of 4.8 years (HR 1.95, 95% CI 1.27; 2.99, $p < 0.01$ for stable CAD and HR 1.95, 95% CI 1.23; 3.11, $p < 0.01$ for ACS).
Conclusion: In a general practice setting, patients with AF had significantly increased adjusted long-term mortality than patients without AF. After publication of the consensus document of different working groups of the European Society of Cardiology in 2010, triple therapy increased markedly.

1. Introduction

Atrial fibrillation (AF) is the most common sustained arrhythmia, occurring in 2–4% of adults greater than 60 years of age and in up to 21% of patients after acute myocardial infarction [1,2].

In the subset of individuals with coronary artery disease (CAD) who develop AF, the following three are factors that may relate to the excess in mortality: First, patients with AF exhibit a significantly higher atherothrombotic risk-profile due to the higher prevalence of co-morbidities, as opposed to patients free of AF. Second, the 3- to 5-fold increased risk of ischemic stroke drives mortality substantially. Third, aggressive antithrombotic therapy, particularly in patients with AF and coronary stenting, accounts directly or indirectly for deaths related to bleeding [3–6].

An optimal antithrombotic strategy in patients requiring triple antithrombotic therapy due to AF and stent implantation (i.e. oral anticoagulation plus dual antiplatelet therapy, DAPT) was first implemented in the 2010 European Society of Cardiology (ESC) Guidelines for the Management of Atrial Fibrillation that were in part based on a consensus document of the working group on thrombosis in cooperation with the European Heart Rhythm Association (EHRA) and European Association of Percutaneous Cardiovascular Interventions (EAPCI) [7,8]. Up to this time point, clear recommendations were lacking and physicians commonly avoided anticoagulation in addition to antiplatelet therapy for safety considerations [6,9,10].

Therefore, we investigated treatment patterns as well as long-term all-cause mortality in patients with acute or stable CAD and concomitant

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AF in a single-center prospective registry in patients undergoing percutaneous coronary intervention (PCI) plus stenting.

2. Methods

In this *post-hoc* analysis of our registry, we collected data about antithrombotic therapy (as used at discretion of the attending cardiologist), cardiovascular risk factors, co-morbidities, and coronary morphology in 3248 consecutive patients undergoing PCI and stenting for an acute coronary syndrome (ACS) or stable CAD between January 2003 and August 2012.

ACS patients presented either with persistent ST-segment elevation myocardial infarction (STEMI) or non ST-elevation acute coronary syndromes (NSTE-ACS). Criteria for STEMI were biomarker evidence of MI with ST-segment elevation of 1 mm or more in two or more contiguous leads, while NSTE-ACS patients required elevated troponin I, troponin T or creatine kinase MB (CK-MB) levels and/or ST-segment depression of $\geq$1 mm for diagnosis. Excluded from this analysis were patients with neither laboratory, nor electrocardiographic evidence suggestive of ACS, as were patients with a paroxysm of AF only during the acute event, and patients in cardiogenic shock or in-hospital death at any time during initial hospitalization (Fig. 1).

AF was defined as irregular rhythm with the lack of distinct atrial activation, as recorded on a 12-lead electrocardiogram.

Informed consent was obtained from each patient. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee (EK 10-046-VK_NZ).

2.1. Clinical endpoints

The primary efficacy endpoint was long-term all-cause mortality and was compared between patients with and without AF, which included new-onset AF or history of AF.

As secondary endpoints, we investigated the proportion of patients treated with either DAPT or triple antithrombotic therapy upon hospital discharge, the proportion of patients receiving drug-eluting stents (DES) in the respective groups, and changes in treatment practices over time.

Mortality data for all patients were obtained from Statistics Austria, an independent and non-profit federal institution under public law that supports scientific services. Cases of death occurring in Austria are centrally recorded by Statistics Austria and data are made available for authorized institutions upon request. For the respective query, patient's name, birth date and gender are matched with the national database in order to identify events of death.

2.2. Statistical methods

Descriptive statistics were performed on baseline variables and stratified by clinical presentation (elective PCI or ACS) and the presence or absence of AF. Discrete characteristics are expressed as frequency counts and percentages, and differences between treatment groups were determined by the Chi-square test. Continuous characteristics are expressed as medians and quartiles, with differences examined using the Mann–Whitney test for the comparison of groups. The level of significance used for all tests was a two-sided p-value of 0.05. A Cox proportional hazard model with step-wise backward elimination using a likelihood-ratio test with a p-level for entry of 0.05 and a p-value for removal 0.2 was applied to determine impact of AF on long-term mortality while controlling for confounders.

Two models were established including the following variables:

1: age, eGFR, BMI, gender, type of stent, diseased vessels, heart failure, prior stroke or TIA, peripheral artery disease, hypertension, hyperlipidemia, smoking, diabetes, prior PCI, prior CABG, prior MI, history for malignancies, statin treatment, STEMI vs. NSTE-ACS (ACS cohort only), and antiplatelet substance (ACS cohort only).
2: as above, including triple therapy vs. DAPT.

We report unadjusted and adjusted outcomes (final Cox proportional hazards model after backward elimination).

Additionally, we performed a 1:1 matched propensity score analysis including the above mentioned variables.

The Software Package for Social Sciences Version 22 (SPSS Inc., Chicago, IL) was used for all statistical calculations.

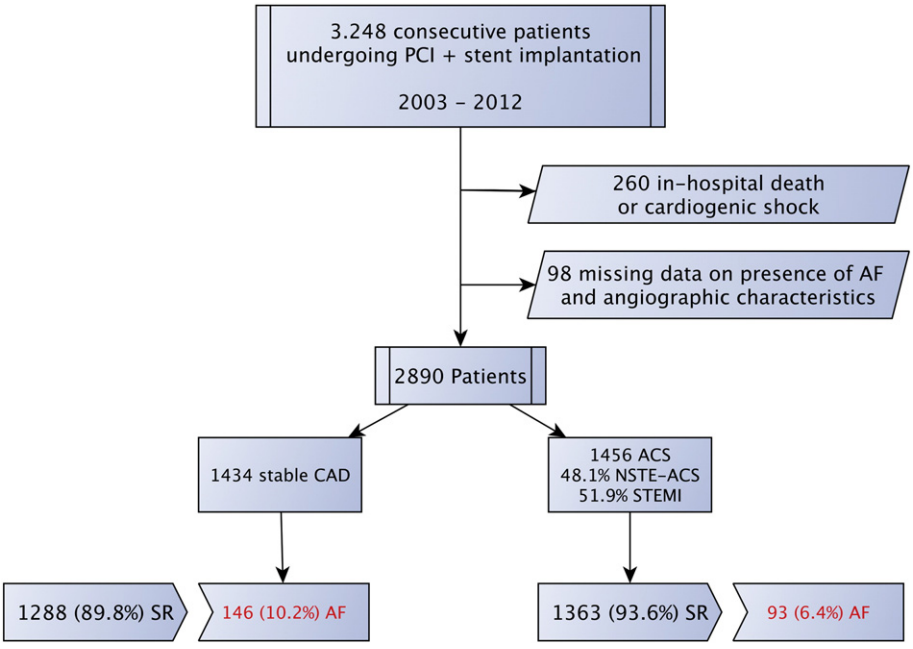

Fig. 1. Selection of patients included into the final analysis: PCI: percutaneous coronary intervention; MI: myocardial infarction; AF: atrial fibrillation; CAD: coronary artery disease; STEMI: ST-elevation myocardial infarction; NSTE-ACS: non-ST-elevation acute coronary syndrome; SR: sinus rhythm.