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Value of DAPT score to predict adverse outcome in patients with atrial fibrillation undergoing percutaneous coronary intervention: A post-hoc analysis from the AFCAS registry☆

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ABSTRACT

Background: The DAPT score identifies patients with expected benefit from extended dual antiplatelet therapy beyond 1 year after percutaneous coronary intervention (PCI). In a post-hoc analysis from the AFCAS registry, we explored the value of DAPT score to predict outcome in patients with atrial fibrillation (AF) undergoing PCI.
Methods and results: Outcome measures included major adverse cardiac/cerebrovascular events (MACCE) [all-cause death, myocardial infarction, repeat revascularization, stent thrombosis, or stroke/transient ischemic attack] and bleeding events. At 12-month follow-up, patients with a DAPT score ≥ 1 had a higher incidence of MACCE, all-cause death, myocardial infarction ($p = 0.004$, $p = 0.006$, and $p = 0.013$, respectively), but a similar bleeding rate ($p = 0.66$), versus those with a DAPT score <1. In a subgroup of patients at high risk of stroke who received triple therapy for 1 month only, DAPT score ≥1 was associated with a higher incidence of MACCE, all-cause death, myocardial infarction ($p = 0.002$, $p = 0.015$, and $p = 0.039$, respectively), but a similar bleeding rate ($p = 0.81$).
Conclusions: In AF patients undergoing PCI, a DAPT score ≥1 was associated with a higher incidence of thrombotic events, and a similar incidence of bleeding events, compared with a DAPT score <1. These results were consistent in patients at high risk of stroke who received triple therapy for 1 month.

1. Introduction

Atrial fibrillation (AF) is the most common sustained arrhythmia with a prevalence of 1–2% in the European Union [1]. Coronary artery disease has been reported in 34% of patients with AF; and 21% need revascularization [2]. The optimal management of antithrombotic therapy in patients with AF who undergo percutaneous coronary intervention (PCI) is unknown. The European Society of Cardiology guidelines on the management of AF recommend that patients with AF who have ≥1 additional stroke risk factor who undergo elective PCI and stenting should receive triple therapy [oral anticoagulation (OAC), clopidogrel, and aspirin] for a short period, followed by a period of dual therapy (OAC plus a single antiplatelet) [3].

These patients frequently have thrombotic and bleeding events shortly after index procedure [4], and thus, there is an unmet clinical need for better risk prediction tools to identify who would benefit from longer versus shorter antiplatelet therapy in addition to OAC. The performance of bleeding risk prediction scores HAS-BLED, ATRIA, mOBRI and REACH was poor in detecting major bleeds in patients with AF undergoing PCI [5].

The DAPT (Dual Antiplatelet Therapy) score is a clinical prediction rule based on ischemic and bleeding risk factors that helps discriminate patients with greater expected benefit versus those with greater expected harm from extended dual antiplatelet therapy beyond 1 year, among

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those who underwent coronary stenting, had no major ischemic or bleeding event within the first year, and were not receiving OAC [6].

In this post-hoc analysis from the AFCAS registry, we explored the value of the DAPT score to predict thrombotic and bleeding events in patients with AF undergoing PCI.

2. Methods

2.1. Patient selection and study design

The AFCAS (Management of patients with Atrial Fibrillation undergoing Coronary Artery Stenting) registry is a prospective multi-center observational study that enrolled consecutive patients with AF who underwent PCI and stenting [4]. The inclusion criterion was ongoing/history of AF (paroxysmal, persistent, or permanent). The only exclusion criteria were unwillingness/inability to participate in the study or to give informed consent. In each participating center, PCI was performed according to local practice, and patients were followed up for 12 months. Peri-procedural and post-procedural antithrombotic regimens were at operator's discretion. Follow-up was performed by telephone calls/clinic visits scheduled at 1, 3, 6, and 12 months after PCI. Patients were enquired about clinical outcome endpoints (described below), hospitalization, and medications. CHA_2DS_2-VASc and HAS-BLED scores were calculated to evaluate the individual risks for stroke and bleeding events, respectively. The DAPT score was calculated as previously described [6]. Briefly, the scoring system assigned 1 point each for myocardial infarction (MI) at presentation, prior MI or PCI, diabetes, stent diameter <3mm, smoking, and paclitaxel-eluting stent; 2 points each for history of congestive heart failure/low ejection fraction and vein graft intervention; −1 point for age 65 to younger than 75 years; and −2 points for age 75 years or older.

2.2. Ethical standards

This investigator-driven study was conducted according to the guidelines of the 1964 Declaration of Helsinki. The study protocol was approved by the ethics committees of the participating centers. Informed written consent was obtained from every patient after full explanation of the study protocol. The AFCAS registry is registered with ClinicalTrials.gov under the identifier: NCT00596570.

2.3. Study definitions and endpoints

The primary outcome measures were: 1) major adverse cardiac/cerebrovascular events (MACCE), and 2) bleeding events during 12-month follow-up. The composite endpoint of MACCE was defined as the first occurrence of all-cause death, MI, repeat revascularization, stent thrombosis, or stroke/transient ischemic attack. MI was defined according to the Third Universal Definition [7]. Repeat revascularization was defined as PCI or coronary bypass surgery to treat significant stenosis (>50%) in the previously treated vessel. Stent thrombosis was adjudicated according to the criteria of definite or probable stent thrombosis described by the Academic Research Consortium [8]. Transient ischemic attack was defined as a transient (<24 h) focal neurological deficit adjudicated by neurologist, whereas stroke was defined as a permanent focal neurological deficit adjudicated by neurologist and confirmed by computed tomography/magnetic resonance imaging. Bleeding events were defined according to the Bleeding Academic Research Consortium (BARC) criteria, and included events adjudicated as minor (BARC 2), and major (BARC 3a, 3b, 3c, and 5) [9].

2.4. Statistical analysis

Continuous variables were reported as the mean ± standard deviation. Categorical variables were described with absolute and relative (percentage) frequencies. Comparisons were performed using the unpaired 2-tailed *t*-test for continuous variables, and the Pearson chi-square test or Fisher Exact test for categorical variables, as appropriate. The calibration of the DAPT score as a continuous variable in predicting 12-month MACCE was assessed using the Hosmer-Lemeshow "goodness-of-fit" test, estimating the calibration slope and assessing the calibration plot, whereas its discrimination ability was assessed using the receiver operating characteristic curve. MACCE at 12 months was considered as a binary endpoint since follow-up at 12 months was completed in all patients, and no competing risk existed. The area under the curve (AUC) with 95% confidence interval (CI) was reported. The Youden's test was used to identify the best cutoff value of the DAPT score that predicts 12-month MACCE. This cutoff value was used to dichotomize the DAPT score. Statistical analyses were performed using SPSS software, version 20 (IBM SPSS Inc., Chicago, IL, USA) and easyROC software (http://www.biosoft.hacettepe.edu.tr/easyROC/).

3. Results

3.1. Baseline characteristics

For the current analysis, we included 929 consecutive patients with AF who underwent PCI between October 2008 and August 2010 at 17 institutions, in 5 European countries. Mean age was 73.0 ± 7.9 years, 276 (29.7%) were females, 460 (49.5%) had permanent AF, 528 (56.8%) were already receiving vitamin K antagonist (VKA) upon enrolment, 529 (56.9%) presented with acute coronary syndrome, 915 (98.5%) were at high risk of stroke (CHA_2DS_2-VASc score >1), 709 (76.3%) were at high pre-estimated risk of bleeding (HAS-BLED score ≥3). Mean peri-procedural International Normalized Ratio was 1.9 ± 0.7.

The DAPT score showed a modest discriminatory ability and good calibration in predicting 12-month MACCE (AUC 0.566, 95%CI 0.522–0.611, Hosmer-Lemeshow test: $p = 0.698$, calibration slope: 0.966) (Supplementary Fig. 1). Youden's test showed that the best cutoff of the DAPT score that predicts MACCE was 1 (sensitivity: 61.7%, specificity 50.2%, negative predictive value 82.5%, positive predictive value 25.6%) (Fig. 1). Further analyses were then performed using this cutoff value.

In the whole cohort, the DAPT score showed normal distribution, with 445 (47.9%) patients having score < 1. Patients with a DAPT score ≥1 had a slightly lower risk of stroke ($p = 0.046$), and a lower risk of bleeding, versus those with a DAPT score <1 ($p < 0.001$) (Supplementary Table 1). At 12-month follow-up, patients with a DAPT score ≥1 had a higher incidence of overall MACCE ($p = 0.004$), all-cause death ($p = 0.006$), and MI ($p = 0.013$), but a similar rate of BARC 2–5 bleeding ($p = 0.66$), compared with those with a DAPT score < 1 (Supplementary Table 2).

Among the whole cohort, 78 (8.4%) had access site complications. In 851 patients without access site complications, the DAPT score also showed normal distribution, with 406 (47.7%) patients having score <1. In this subgroup of patients, those with a DAPT score ≥1 had a slightly lower risk of stroke ($p = 0.03$), and a lower risk of bleeding ($p < 0.001$), compared with those with a DAPT score <1 (Supplementary Table 3). At 12-month follow-up, patients with a DAPT score ≥1 had a higher incidence of overall MACCE ($p = 0.002$), all-cause death ($p = 0.004$), and MI ($p = 0.005$), but a similar rate of BARC 2–5 bleeding ($p = 0.25$), compared with those with DAPT score < 1 (Supplementary Table 4).

Among 851 patients without access site complications, 307 (36.1%) patients received triple therapy (VKA, clopidogrel, and aspirin) for 1 month only. In these 307 patients, the DAPT score again showed normal distribution, with 167 (54.4%) patients having score <1. Moreover, in these patients, those with a DAPT score ≥1 had a lower risk of bleeding ($p = 0.001$), but had a similar risk of stroke ($p = 1.0$), compared with those with a DAPT score <1 (Table 1). Among these 307