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Duration of Triple Antithrombotic Therapy and Outcomes Among Patients Undergoing Percutaneous Coronary Intervention

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ABSTRACT

OBJECTIVES The aim of this study was to compare clinical outcomes in relation to the duration of triple antithrombotic therapy (TAT) among patients with indications for oral anticoagulation undergoing percutaneous coronary intervention (PCI).

BACKGROUND TAT is recommended for patients undergoing PCI with a firm indication for oral anticoagulation. Duration of TAT may influence outcomes, but the optimal period of TAT remains uncertain.

METHODS Between 2009 and 2013, 8,772 consecutive patients undergoing PCI for stable coronary artery disease or acute coronary syndrome were prospectively included in the Bern PCI Registry (NCT02241291). Of 568 patients with indications for oral anticoagulation, 245 (43%) were discharged on a regimen of 1-month TAT and 323 (57%) on a regimen >1-month TAT (mean 5.1 ± 3.3 months, median 3 months). The primary endpoint was a composite of cardiac death, myocardial infarction, stroke, definite stent thrombosis, or TIMI (Thrombolysis in Myocardial Infarction) major bleeding within 1 year.

RESULTS Patients on 1-month compared with >1-month TAT were more commonly women, with stable coronary artery disease, had higher HAS-BLED scores, and less frequently received drug-eluting stents. In multivariate analyses, the primary endpoint did not differ between groups (adjusted hazard ratio: 1.07; 95% confidence interval: 0.56 to 2.06; $p = 0.84$). Results were consistent in stratified analyses in relation to clinical presentation with acute coronary syndrome (38%) and PCI with drug-eluting stents (79%) (p for interaction = 0.18 and 0.95, respectively). There were no differences in the secondary bleeding endpoint, Bleeding Academic Research Consortium ≥3 bleeding (adjusted hazard ratio: 0.62; 95% confidence interval: 0.21 to 1.80; $p = 0.37$) and the secondary composite ischemic endpoint (cardiac death, myocardial infarction, stroke, or definite stent thrombosis) (adjusted hazard ratio: 1.12; 95% confidence interval: 0.55 to 2.29; $p = 0.76$).

CONCLUSIONS One-month TAT, used preferentially in patients with higher estimated bleeding risk in this observational study, was associated with similar net clinical outcomes compared with longer TAT durations throughout 1 year following PCI. (J Am Coll Cardiol Intv 2016;9:1473–83) © 2016 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndrome(s)

AF = atrial fibrillation

BMS = bare-metal stent(s)

CAD = coronary artery disease

CI = confidence interval

DAPT = dual-antiplatelet therapy

DES = drug-eluting stent(s)

HR = hazard ratio

MI = myocardial infarction

OAC = oral anticoagulation

PCI = percutaneous coronary intervention

TAT = triple antithrombotic therapy

Up to 10% of patients undergoing percutaneous coronary intervention (PCI) have concomitant indications for oral anticoagulation (OAC) (1,2). The therapeutic targets of OAC protecting against ischemic complications related to fibrin-rich thrombus in patients with atrial fibrillation (AF) or mechanical valves (3,4) versus dual-antiplatelet therapy (DAPT) for prevention of platelet-dependent stent thrombosis (5,6) are complementary and dependent on different pathobiological pathways. Therefore, a combination of OAC plus DAPT is plausible among patients with indications for OAC undergoing PCI and is currently recommended in consensus documents (1,7–9). Triple antithrombotic therapy (TAT), the combination of OAC and DAPT, is associated with increased bleeding risk (10,11) but is more effective than DAPT alone for reduction of major adverse cardiovascular events in these patients (1,12,13).

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Less intensive antithrombotic regimens (e.g., omission of aspirin) have received attention as a potential means of mitigating bleeding risk (14–16) and may be considered as an alternative to TAT in selected patients (1,7,8). Abbreviated regimens of TAT may be explored as an alternative strategy to optimize the benefit-to-risk ratio in view of the fact that bleeding associated with TAT appears to be exposure dependent and related to treatment duration (17). In this context, the ISAR-TRIPLE (Intracoronary Stenting and Antithrombotic Regimen–Testing of a 6-Week Versus a 6-Month Clopidogrel Treatment Regimen in Patients With Concomitant Aspirin and Oral Anticoagulant Therapy Following Drug-Eluting Stenting) randomized trial reported comparable net clinical outcomes with 6-week versus 6-month TAT following PCI with drug-eluting stent (DES), supporting the role of shorter TAT duration in this setting (18). The length of TAT is currently recommended to be adjusted according to individual thrombotic and bleeding risk, clinical presentation, and type of stent; these recommendations remain largely consensus rather than evidence based, as reflected by the low level of evidence and differences between European (1,7,8) and North American guidelines regarding specific TAT durations (19).

Against this background, the purpose of the present observational study was to compare clinical outcomes in relation to a regimen of 1-month versus more prolonged TAT in a cohort of unselected patients undergoing PCI with indications for OAC.

METHODS

PATIENT POPULATION. This was a retrospective analysis of prospectively collected data. All consecutive patients undergoing PCI for stable coronary artery disease (CAD) or acute coronary syndrome (ACS) at Bern University Hospital (Bern, Switzerland) as of 2009 were prospectively entered into the Bern PCI Registry (NCT02241291). The present analysis included all consecutive patients with clinical indications for OAC who were discharged on TAT. Per default, most patients requiring OAC at our institution receive additional DAPT of differing duration following PCI instead of less intensive antithrombotic regimens (e.g., OAC plus antiplatelet monotherapy). In line with the inclusive character of the registry, there were no formal exclusion criteria. Demographic and clinical characteristics, information on performed interventions, and hospital outcome data were systematically collected. Scores of HAS-BLED (hypertension, abnormal liver or renal function, stroke or thromboembolism, bleeding history, elderly [age >65 years], drug consumption or alcohol abuse) were calculated, excluding labile international normalized ratio values, which were not collected. The registry was approved by the institutional ethics committee, and patients provided written informed consent to undergo prospective follow-up.

PROCEDURES. PCI was performed in accordance with current practice guidelines (7). Periprocedural management, including interrupted versus uninterrupted OAC, dose of unfractionated heparin, or use of glycoprotein IIb/IIIa inhibitors, was left to the discretion of the operator. DAPT consisting of acetylsalicylic acid and a $P2Y_{12}$ inhibitor was initiated before, at the time of, or immediately after the procedure. The $P2Y_{12}$ inhibitor of choice was clopidogrel in the majority of patients. Ticagrelor or prasugrel was administered if deemed clinically necessary by the treating physician in certain cases of ACS, complex anatomy, or complicated interventions; prasugrel was selectively used before the excessive bleeding risk for TAT including prasugrel was reported (20). The duration of DAPT was not uniformly specified but individualized accounting for each patient's clinical presentation, ischemic and bleeding risk profile.

PATIENT FOLLOW-UP. Patients were systematically followed at discharge and throughout 1 year to assess adverse cardiac and cerebrovascular events. Survival data were obtained from hospital records and municipal civil registries. A health questionnaire was sent to all living patients with questions on rehospitalization, medical treatment, and adverse events,