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CME

Triple Therapy With Aspirin, Prasugrel, and Vitamin K Antagonists in Patients With Drug-Eluting Stent Implantation and an Indication for Oral Anticoagulation

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JACC JOURNAL CME

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CME Objective for This Article: At the conclusion of this activity, the learner should be able to evaluate whether prasugrel may serve as an alternative to clopidogrel in patients with triple therapy.

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Triple Therapy With Aspirin, Prasugrel, and Vitamin K Antagonists in Patients With Drug-Eluting Stent Implantation and an Indication for Oral Anticoagulation

Objectives This study sought to evaluate whether prasugrel may serve as an alternative to clopidogrel in patients with triple therapy.

Background Approximately 10% of patients who receive dual antiplatelet therapy after percutaneous coronary intervention have an indication for oral anticoagulation and are thus treated with triple therapy. The standard adenosine diphosphate receptor blocker in this setting is clopidogrel. Data regarding prasugrel as part of triple therapy are not available.

Methods We analyzed a consecutive series of 377 patients who underwent drug-eluting stent implantation and had an indication for oral anticoagulation between February 2009 and December 2011 and were treated with a 6-month regimen of aspirin and oral anticoagulation with either prasugrel or clopidogrel. The primary endpoint was a composite of Thrombolysis In Myocardial Infarction (TIMI) major and minor bleeding at 6 months. The secondary endpoint was a composite of death, myocardial infarction, ischemic stroke, or definite stent thrombosis.

Results Twenty-one patients (5.6%) received prasugrel instead of clopidogrel. These patients had a higher-risk profile at baseline, and the majority had high platelet reactivity to clopidogrel. TIMI major and minor bleeding occurred significantly more often in the prasugrel compared with the clopidogrel group (6 [28.6%] vs. 24 [6.7%]; unadjusted hazard ratio (HR): 4.6, 95% confidence interval [CI]: 1.9 to 11.4], $p < 0.001$; adjusted HR: 3.2, 95% CI: 1.1 to 9.1], $p = 0.03$). There was no significant difference regarding the combined ischemic secondary endpoint (2 [9.5%] vs. 25 [7.0%]; unadjusted HR: 1.4, 95% CI: 0.3 to 6.1], $p = 0.61$).

Conclusions These findings suggest that substitution of prasugrel for clopidogrel in patients needing triple therapy increases the risk of bleeding. However, specific randomized trials are needed to define the role of newer adenosine diphosphate receptor antagonists in this setting. (J Am Coll Cardiol 2013;61:2060–6) © 2013 by the American College of Cardiology Foundation

Approximately 5% to 10% of patients undergoing coronary stenting have an additional indication for oral anticoagulation (OAC) (1) and will thus require a so-called triple therapy consisting of aspirin, OAC, and an adenosine diphosphate (ADP) receptor antagonist. The most common combination currently consists of aspirin, clopidogrel, and a vitamin K antagonist.

Data from retrospective studies revealed that there is a 3- to 5-fold increase in bleeding rates associated with this triple therapy compared with various combinations of dual therapy (2–8). When it comes to ischemic outcomes, however, a meta-analysis of nonrandomized studies suggested that triple therapy is more efficacious than dual antiplatelet therapy in the prevention of major adverse cardiovascular events and that there is a significant reduction in all-cause mortality (9). Current guidelines therefore advocate triple therapy in patients on OAC undergoing coronary stent implantation (10,11).

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For years clopidogrel has been the standard antiplatelet agent after coronary stent implantation because of its good safety and efficacy profile (12,13). Its downside, however, is its nonuniform and rather slow transformation to its active metabolite, leading to a substantial number of patients who display on-treatment high platelet reactivity (HPR), a condition associated with a significant increase in ischemic events (14). Newer antiplatelet drugs such as prasugrel (15,16) have therefore been developed to overcome clopidogrel's limitations and recent percutaneous coronary intervention (PCI) guidelines suggest that prasugrel might be considered an alternative agent in patients treated with clopidogrel with HPR (12). However, data regarding prasugrel as part of triple therapy are not available.

The purpose of our study was therefore to evaluate whether prasugrel may serve as an alternative to clopidogrel in patients with an indication for OAC and drug-eluting stent (DES) implantation.

Methods

Study population. This is an analysis of prospectively collected data on patients who presented at Deutsches Herzzentrum and 1. Medizinische Klinik, Klinikum rechts der Isar, both in Munich, Germany, between February 2009, when prasugrel was approved in Europe, and December 2011. All patients who underwent DES placement and were discharged with a 6-month regimen of aspirin, OAC with phenprocoumon, and an ADP antagonist were included. In stable patients on OAC who underwent PCI, the procedure was postponed until international normalized ratio (INR) values were ≤2. In general, bridging therapy was not performed unless patients had a high thromboem-