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Novel Approaches for Preventing or Limiting Events (Naples) III Trial

Randomized Comparison of Bivalirudin Versus Unfractionated Heparin in Patients at Increased Risk of Bleeding Undergoing Transfemoral Elective Coronary Stenting

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CME Objective for This Article: At the completion of this article, the learner should be able to: 1) identify current recommendations for lowering the peri-procedural bleeding risk without compromising the risk of ischemic complications; 2) explain the lower than expected major bleeding rate in the unfractionated heparin group that was observed in this trial; and 3) discuss the cost-effectiveness of sub.

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ABSTRACT

OBJECTIVES This study sought to assess the safety and the efficacy of bivalirudin compared with unfractionated heparin (UFH) alone in the subset of patients at increased risk of bleeding undergoing transfemoral elective percutaneous coronary intervention (PCI).

BACKGROUND Bivalirudin, a synthetic direct thrombin inhibitor, determines a significant decrease of in-hospital bleeding following PCI.

METHODS This is a single-center, investigator-initiated, randomized, double-blind, controlled trial. Consecutive biomarker-negative patients at increased bleeding risk undergoing PCI through the femoral approach were randomized to UFH (UFH group; n = 419) or bivalirudin (bivalirudin group; n = 418). The primary endpoint was the rate of in-hospital major bleeding.

RESULTS The primary endpoint occurred in 11 patients (2.6%) in the UFH group versus 14 patients (3.3%) in the bivalirudin group (odds ratio: 0.78; 95% confidence interval: 0.35 to 1.72; p = 0.54). Distribution of access-site and non–access-site bleeding was 18% and 82% in the UFH group versus 50% and 50% in the bivalirudin group (p = 0.10).

CONCLUSIONS The results of this randomized study, carried out at a single institution, suggest that there is no difference in major bleeding rate between bivalirudin and UFH in increased-risk patients undergoing transfemoral PCI. (Novel Approaches in Preventing and Limiting Events III Trial: Bivalirudin in High-Risk Bleeding Patients [NAPLES III]; NCT01465503) (J Am Coll Cardiol Intv 2015;8:414–23) © 2015 by the American College of Cardiology Foundation.

An anticoagulant should be administered to patients undergoing percutaneous coronary intervention (PCI) in order to limit ischemic complications (1,2). However, this approach may increase the risk of bleeding (1), which have been strongly associated with in-hospital and late major adverse events (3–6). Even with its intrinsic and well-recognized limitations (7,8), unfractionated heparin (UFH) is still the most commonly used anticoagulant drug during PCI. Bivalirudin is a synthetic direct thrombin inhibitor with several favorable properties, including its ability to inhibit both circulating and clot-bound thrombin, an inherent antiplatelet effect (by inhibition of thrombin-induced platelet activation), a linear kinetics and a short half-life (9–11). It has been shown that systematic use of bivalirudin decreases bleeding, ensuring similar protection against ischemic events both in acute (9–13) and in elective (14,15) settings. At present, there is a lack of prospective, randomized clinical trials assessing the safety and the efficacy of bivalirudin compared with UFH in the subset of biomarker-negative patients at increased bleeding risk undergoing PCI. The NAPLES (Novel Approaches for Preventing or Limiting Events) III trial was designed to test the hypothesis that bivalirudin, compared with UFH, may provide significant benefits in term of bleeding in the selected population of biomarker-negative patients who are deemed at increased risk of bleeding and are undergoing transfemoral PCI.

METHODS

The NAPLES III trial is a prospective, investigator-initiated, double-blind, randomized controlled trial carried out at the Clinica Mediterranea, Naples, Italy. The trial has been registered with Clinicaltrials.gov (NCT01465503). The design of the NAPLES III trial has been previously reported (16). From January 14, 2008, to December 7, 2012, consecutive