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Bivalirudin or Heparin in Patients Undergoing Invasive Management of Acute Coronary Syndromes

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ABSTRACT

BACKGROUND Contrasting evidence exists on the comparative efficacy and safety of bivalirudin and unfractionated heparin (UFH) in relation to the planned use of glycoprotein IIb/IIIa inhibitors (GPIs).

OBJECTIVES This study assessed the efficacy and safety of bivalirudin compared with UFH with or without GPIs in patients with acute coronary syndrome (ACS) who underwent invasive management.

METHODS In the MATRIX (Minimizing Adverse Haemorrhagic Events by Transradial Access Site and Systemic Implementation of AngioX) program, 7,213 patients were randomly assigned to receive either bivalirudin or UFH with or without GPIs at discretion of the operator. The 30-day coprimary outcomes were major adverse cardiovascular events (MACEs) (a composite of death, myocardial infarction, or stroke), and net adverse clinical events (NACEs) (a composite of MACEs or major bleeding).

RESULTS Among 3,603 patients assigned to receive UFH, 781 (21.7%) underwent planned treatment with GPI before coronary intervention. Bailout use of GPIs was similar between the bivalirudin and UFH groups (4.5% and 5.4%) ($p = 0.11$). At 30 days, the 2 coprimary endpoints of MACEs and NACEs, as well as individual endpoints of mortality, myocardial infarction, stent thrombosis or stroke did not differ among the 3 groups after adjustment. Compared with the UFH and UFH+GPI groups, bivalirudin reduced bleeding, mainly the most severe bleeds, including fatal and nonaccess site–related events, as well as transfusion rates and the need for surgical access site repair. These findings were not influenced by the administered intraprocedural dose of UFH and were confirmed at multiple sensitivity analyses, including the randomly allocated access site.

CONCLUSIONS In patients with ACS, the rates of MACEs and NACEs were not significantly lower with bivalirudin than with UFH, irrespective of planned GPI use. However, bivalirudin significantly reduced bleeding complications, mainly those not related to access site, irrespective of planned use of GPIs. (Minimizing Adverse Haemorrhagic Events by Transradial Access Site and Systemic Implementation of AngioX [MATRIX]; NCT01433627) (J Am Coll Cardiol 2018;71:1231–42) © 2018 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndrome(s)

CABG = coronary artery bypass grafting

GPI = glycoprotein IIb/IIIa inhibitor

MACE = major adverse cardiovascular event

NACE = net adverse clinical event

NSTE-ACS = non–ST-segment elevation acute coronary syndrome(s)

PCI = percutaneous coronary intervention

ST = stent thrombosis

TIMI = Thrombolysis In Myocardial Infarction

UFH = unfractionated heparin

The most effective antithrombotic therapy in patients with an acute coronary syndrome (ACS) who are undergoing a percutaneous coronary intervention (PCI) remains strongly debated (1–3). Unfractionated heparin (UFH) (with or without planned glycoprotein IIb/IIIa inhibitors [GPIs]) and bivalirudin are 2 of the most commonly used antithrombotic strategies and have been compared in different trials since the 1990s (4). Conflicting data have accumulated since then, so that the comparative safety and effectiveness profile of bivalirudin compared with UFH alone in current practice remains unclear.

Although some trials, including EUROMAX (European Ambulance Acute Coronary Syndrome Angiography Trial) (5,6) and BRIGHT (Bivalirudin in Acute Myocardial Infarction vs Heparin and GPI Plus Heparin Trial) (7), have shown benefits in terms of major bleeding reduction related to bivalirudin use, irrespective of GPI use in the UFH arm, the HEAT-PPCI (How Effective are Antithrombotic Therapies in Primary Percutaneous Coronary Intervention) and the most recent VALIDATE-SWEDEHEART (Bivalirudin versus Heparin in ST-Segment and Non-ST-Segment Elevation Myocardial Infarction in Patients on Modern Antiplatelet Therapy in the Swedish Web System for Enhancement and Development of Evidence-based Care in Heart Disease Evaluated according to Recommended Therapies Registry Trial) studies showed that heparin alone did not increase bleeding events compared with bivalirudin (8,9). Because planned use of GPIs in patients who receive UFH has been reduced, this discrepancy is notable.

SEE PAGE 1243

Therefore, we pre-specified to examine the comparative efficacy and safety profile of bivalirudin compared with UFH alone or with UFH+GPI in the context of the largest contemporary trial to assess the value of bivalirudin in an all-comer ACS population and the only study that allocated access site by random selection.

METHODS

STUDY DESIGN. The MATRIX (Minimizing Adverse Haemorrhagic Events by Transradial Access Site and Systemic Implementation of AngioX) antithrombin study is a randomized, multicenter trial that compared bivalirudin (the use of GPIs was restricted

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