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The Prognostic Value of Bleeding Academic Research Consortium (BARC)-Defined Bleeding Complications in ST-Segment Elevation Myocardial Infarction

A Comparison With the TIMI (Thrombolysis In Myocardial Infarction), GUSTO (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries), and ISTH (International Society on Thrombosis and Haemostasis) Bleeding Classifications

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Objectives The aim of the present analysis was to compare 1-year mortality prediction of Bleeding Academic Research Consortium (BARC)-defined bleeding complications with existing bleeding definitions in patients with ST-segment elevation myocardial infarction (STEMI) and to investigate the prognostic value of the individual data elements of the bleeding classifications for 1-year mortality.

Background BARC recently proposed a novel standardized bleeding definition.

Methods The in-hospital occurrence of bleeding defined according to the BARC, TIMI (Thrombolysis In Myocardial Infarction), GUSTO (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries), and ISTH (International Society on Thrombosis and Haemostasis) bleeding classifications was assessed in 2,002 STEMI patients undergoing primary percutaneous coronary intervention between January 1, 2003, and July 31, 2008.

Results BARC types 2, 3, 4, and 5 bleeding occurred in 4.4%, 14.2%, 1.4%, and 0.3% of patients, respectively. By multivariable analysis, GUSTO- and ISTH-defined bleeding was not significantly associated with 1-year mortality, whereas TIMI major and BARC type 3b or 3c bleeding conferred a 2-fold higher risk of 1-year mortality (hazard ratios [HRs]: 2.00 [95% confidence interval (CI): 1.32 to 3.01] and 1.84 [95% CI: 1.23 to 2.77], respectively). Data elements most strongly associated with mortality were a hemoglobin decrease ≥5 g/dl (HR: 1.94 [95% CI: 1.26 to 2.98]), the use of vasoactive agents for bleeding (HR: 2.01 [95% CI: 0.91 to 4.44]), cardiac tamponade (HR: 2.38 [95% CI: 0.56 to 10.1]), and intracranial hemorrhage (HRs for 1-year mortality were not computable because there was only 1 patient with intracranial bleeding).

Conclusions Both the BARC and TIMI bleeding classification identified STEMI patients at risk of 1-year mortality. (J Am Coll Cardiol 2014;63:1866–75) © 2014 by the American College of Cardiology Foundation

Antithrombotic therapy in conjunction with primary percutaneous coronary intervention (PPCI) reduces the risk of recurrent ischemic events and death in patients with

See page 1876

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ST-segment elevation myocardial infarction (STEMI), at the expense of an increase in iatrogenic bleeding complications (1,2). Major bleeding complications in patients undergoing percutaneous coronary intervention (PCI) and in patients with acute coronary syndromes are associated with short-term mortality and morbidity, prolonged length of stay, and greater resource consumption (3–5). Consequently, inclusion of bleeding as a safety endpoint in randomized controlled trials has become pivotal for the assessment of new antithrombotic agents and interventional techniques. In previous studies, a broad variety of bleeding classifications have been used to report hemorrhagic complications. This variety has hampered direct comparison of the incidence of bleeding complications across different trials or even within studies, because reported bleeding events may vary widely according to the bleeding definition applied (6).

BARC (Bleeding Academic Research Consortium) has recently developed a standardized hierarchical bleeding classification system (7). The prognostic value of BARC-defined bleeding complications was recently established in patients with non–ST-segment elevation acute coronary syndrome and in patients undergoing elective PCI but has not been investigated in high-risk patients, such as in those with STEMI (8). Furthermore, it is of particular interest to investigate the prognostic impact of the individual data elements that comprise the BARC and other bleeding classifications because this might contribute to further optimizing bleeding definitions (9,10). Therefore, the aim of the present study was: 1) to investigate the relationship of BARC bleeding with 30-day and 1-year mortality; 2) to investigate how the BARC bleeding definition compares with existing bleeding definitions with regard to mortality prediction; and 3) to investigate the incidence and prognostic value of the separate bleeding data elements that comprise the bleeding definitions.

Methods

Source population and procedures. The data analyzed in this study were obtained from STEMI patients accepted for PPCI at the Academic Medical Center, University of Amsterdam, between January 1, 2003, and July 31, 2008. The study complied with the principles of the Declaration of Helsinki, and the local ethics committee approved the study protocol. In general, patients qualified for PPCI if they had typical ischemic chest pain and at least a 1-mm ST-segment elevation in 2 or more contiguous leads, a new left bundle branch block, or a true posterior myocardial infarction. Patients received a standard 300- to 600-mg loading dose of clopidogrel. If a coronary stent was implanted, clopidogrel was prescribed for at least 1 month to patients with a bare metal stent and for 6 to 12 months to patients with a drug-eluting stent. Patients were routinely pretreated with 300 mg of aspirin and 5,000 IU of unfractionated heparin. An additional heparin bolus was administered at the catheterization laboratory if necessary to achieve a targeted activated clotting time of 300 s followed by an infusion of 12 U/kg/h with titration to achieve a target activated partial thromboplastin time (aPTT) of 1.5 to 2.0 times the control. Glycoprotein IIb/IIIa inhibitors were used at the discretion of the operator.

Procedural and angiographic data were prospectively collected and entered into a dedicated database by interventional cardiologists and specialized nurses. Chart review for consecutive STEMI patients with available aPTT measurements was performed in the context of a study designed to investigate the relationship between aPTT and clinical outcome in STEMI patients treated with PPCI. A detailed description of the study protocol has been published previously (11). Source documentation (laboratory results, discharge letters, case history, and nurse reports) was collected for every hospital admission for each patient in both the PCI center and in referring hospitals and was assessed for the occurrence of clinical events, including hemorrhage. Follow-up information regarding vital status was obtained from computerized, long-term mortality records from the Dutch National Death Index between January 1, 2012, and April 30, 2012.

Abbreviations and Acronyms

aPTT = activated partial thromboplastin time
BARC = Bleeding Academic Research Consortium
CABG = coronary artery bypass graft
GUSTO = Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries
IDI = integrated discrimination improvement
ISTH = International Society on Thrombosis and Haemostasis
NRI = net reclassification improvement
PCI = percutaneous coronary intervention
PPCI = primary percutaneous coronary intervention
STEMI = ST-segment elevation myocardial infarction
TIMI = Thrombolysis In Myocardial Infarction

STUDY DESIGN, BLEEDING DEFINITIONS, AND ADJUDICATION. The study cohort consisted of all STEMI patients included in our study database who were alive at the end of the procedure. The primary outcome of this study was 1-year all-cause mortality. All hospitalizations were reviewed for the presence of bleeding by 1 author (W.J.K.) who had full access to the patient's clinical and laboratory records. Complicated cases were discussed and adjudicated with 2 other authors (J.G.P.T. and J.P.S.H.). For each bleeding event, the following items were recorded in the study database: the date and source of the bleeding, the hemoglobin decrease associated with the bleeding event (adjusted for the amount of transfusions), the amount of blood transfusions attributable to the bleeding event, the discontinuation of antithrombotic therapy associated with bleeding (as well as the use of aspirin, thienopyridine, vitamin K antagonists, heparin, and glycoprotein IIb/IIIa inhibitors before and after the bleeding was recorded), use of diagnostic procedures (including imaging techniques), surgery to control bleeding, the use of vasoactive agents for bleeding,