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1-Year Outcomes With Intracoronary Abciximab in Diabetic Patients Undergoing Primary Percutaneous Coronary Intervention

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ABSTRACT

BACKGROUND Diabetic patients are at increased risk for future cardiovascular events after ST-segment elevation myocardial infarction (STEMI). Administration of an intracoronary abciximab bolus during primary percutaneous coronary intervention (PCI) may be beneficial in this high-risk subgroup.

OBJECTIVES This study sought to report the 1-year clinical outcomes and cardiac magnetic resonance (CMR) findings in STEMI patients with and without diabetes randomized to intracoronary or intravenous abciximab bolus at the time of primary PCI.

METHODS Patient-level data from 3 randomized trials were pooled. The primary endpoint was the composite of death or reinfarction. Comprehensive CMR imaging was performed in 1 study.

RESULTS Of 2,470 patients, 473 (19%) had diabetes and 1,997 (81%) did not. At 1 year, the primary endpoint was significantly reduced in diabetic patients randomized to intracoronary abciximab compared with those randomized to intravenous bolus (9.2% vs. 17.6%; hazard ratio [HR]: 0.49; 95% confidence interval [CI]: 0.28 to 0.83; p = 0.009). The intracoronary abciximab bolus did not reduce the primary endpoint in patients without diabetes (7.4% vs. 7.5%; HR: 0.95; 95% CI: 0.68 to 1.33; p = 0.77), resulting in a significant interaction (p = 0.034). Among diabetic patients, intracoronary versus intravenous abciximab bolus was associated with a significantly reduced risk of death (5.8% vs. 11.2%; HR: 0.51; 95% CI: 0.26 to 0.98; p = 0.043) and definite/probable stent thrombosis (1.3% vs. 4.8%; HR: 0.27; 95% CI: 0.08 to 0.98; p = 0.046). At CMR (n = 792), the myocardial salvage index was significantly increased only in diabetic patients randomized to intracoronary compared with intravenous abciximab (54.4; interquartile range: 35.1 to 78.2 vs. 39.0, interquartile range: 24.7 to 61.7; p = 0.011; p for interaction vs. no diabetes = 0.016).

CONCLUSIONS In diabetic patients with STEMI, the administration of intracoronary abciximab improved the effectiveness of primary PCI compared with the intravenous bolus. (J Am Coll Cardiol 2016;68:727–38)

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ABBREVIATIONS AND ACRONYMS

CI = confidence intervals

CMR = cardiac magnetic resonance

GPI = glycoprotein IIb/IIIa receptor inhibitors

HR = hazard ratio

IQR = interquartile range

PCI = percutaneous coronary intervention

STEMI = ST-segment elevation myocardial infarction

The global burden of diabetes has risen dramatically over the past 2 decades, and the worldwide prevalence of this disease is yet expected to increase by more than 50% in the next 20 years (1). Acute myocardial infarction remains the most common diabetes-related complication, due to a balance between the steady decline in its incidence and the increase in life expectancy and population growth (2). Although the widespread adoption of primary percutaneous coronary intervention (PCI) marked an important milestone in the treatment of ST-segment elevation myocardial infarction (STEMI), diabetic patients continue to be at high risk for recurrent ischemic events following primary PCI, with a mortality rate exceeding 10% at 1 year (3).

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The pathobiology of atherothrombosis in diabetic patients is likely multifactorial. Among several pathways that are involved, enhanced platelet reactivity is central to the predisposition to thrombosis in diabetes (4,5). Indeed, converging lines of evidence indicate that antithrombotic therapy, including new $P2Y_{12}$ receptor inhibitors, glycoprotein IIb/IIIa receptor inhibitors (GPI), and, more recently, protease-activated receptor-1 antagonists afford a greater absolute, or even relative benefit in diabetic compared with nondiabetic patients (6–9).

The intracoronary bolus of abciximab, the first agent within the GPI class, has the potential to further improve the effectiveness of mechanical reperfusion in diabetic patients with STEMI by combining potent inhibition of platelet activation, similar to the intravenous route, with the advantage of a high drug load and immediate onset of action at the culprit site (10).

Our objective was to investigate the 1-year outcomes of intracoronary versus intravenous abciximab bolus in diabetic versus nondiabetic patients with STEMI undergoing primary PCI in a pooled analysis of 3 randomized trials.

METHODS

STUDY DESIGN AND PATIENT POPULATION. Methodological aspects of the present patient-level pooled analysis were reported elsewhere (10). All principal investigators provided individual patient data using an anonymized electronic dataset. All data were checked for completeness and consistency, and compared with the results of original publications.

The present study was designed to evaluate the 1-year follow-up associated with intracoronary and intravenous abciximab bolus. From the initial population of 3,158 patients, 2 studies (n = 688) were excluded because the follow-up was only 30 days, leaving 2,470 patients enrolled across 3 randomized trials for this analysis (11–13).

Cardiac magnetic resonance (CMR) data of patients included in the imaging substudy of the AIDA STEMI (Abciximab Intracoronary versus intravenously Drug Application in STEMI) trial were analyzed as well (14). Details of the substudy design and CMR methods were previously reported (14). In brief, consecutive patients enrolled at 8 sites in the AIDA STEMI trial were included in the CMR substudy. Per protocol, CMR was performed with a clinical 1.5- or 3.0-T magnetic resonance scanner on days 1 to 10 after the index event, and a CMR core laboratory blindly assessed imaging data. For all quantitative analyses, certified CMR evaluation software was used (cmr^{42}, Circle Cardiovascular Imaging, Calgary, Canada).

All patients had a diagnosis of STEMI and were admitted within 12 h of symptom onset. Dual antiplatelet therapy included aspirin and clopidogrel (300- to 600-mg loading dose followed by 75 mg daily) or prasugrel (60-mg loading dose followed by 10 mg daily). Periprocedural anticoagulation consisted of intravenous unfractionated heparin in all cases. Patients were randomized to receive either an intracoronary or an intravenous bolus of abciximab (0.25 mg/kg body weight) at the time of primary PCI. In patients randomized to the intracoronary route, the abciximab bolus was administered through the guiding catheter after wiring the infarct-related artery. Irrespective of the allocated treatment, patients received an intravenous abciximab infusion for 12 h at 0.125 μg/kg/min. Diabetes was defined as known diabetes at hospital admission.

All trials included in our analysis complied with the provisions of the Declaration of Helsinki, and the ethics committees at each study center approved the study protocols. All patients provided written informed consent for participation in the individual studies.

STUDY ENDPOINTS AND FOLLOW-UP. The primary clinical endpoint was the composite of death or reinfarction at the 1-year follow-up. The secondary endpoints included death, reinfarction, stent thrombosis, and in-hospital bleeding. Stent thrombosis was defined according to the Academic Research Consortium criteria. In-hospital bleeding was classified as moderate/severe according to GUSTO (Global Utilization of Streptokinase and Tissue Plasminogen