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Intracoronary abciximab in diabetic patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention☆

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ABSTRACT

Background: Although intracoronary abciximab failed to improve prognosis compared with intravenous route in unselected ST-segment elevation myocardial infarction (STEMI) patients, little is known about the role of intracoronary abciximab in diabetic patients.
Objectives: To evaluate the efficacy of intracoronary abciximab administration in diabetic patients with STEMI undergoing primary percutaneous coronary intervention (PCI).
Methods: Reperfusional and clinical outcomes of intracoronary abciximab compared with intravenous bolus abciximab according to diabetic status were evaluated in a pooled analysis of five randomized trials including 3158 STEMI patients. The primary clinical endpoint of the study was the composite of death or reinfarction at 30-day follow-up.
Results: Among 584 diabetic patients (18.5%), the composite of death or reinfarction was significantly reduced with intracoronary abciximab compared to intravenous abciximab (4.7% vs. 8.8%; rate ratio [RR], 0.50; 95% confidence intervals [CI], 0.26–0.99; p = 0.04), driven by numerically lower deaths (3.7% vs. 6.4%; RR, 0.56; 95% CI, 0.26–1.20; p = 0.13). Moreover, a significant reduction in definite or probable stent thrombosis was observed in patients receiving intracoronary abciximab (1% vs. 3.5%; RR, 0.27; 95% CI, 0.07–0.99; p = 0.04). Although formal tests for interaction were not significant, no clinical benefit was apparent in the cohort of STEMI patients without diabetes (n = 2574).
Conclusions: In diabetic patients with STEMI undergoing primary PCI, intracoronary abciximab may improve clinical outcomes as compared with standard intravenous use. These findings require confirmation in a dedicated randomized trial.

1. Introduction

Primary percutaneous coronary intervention (PCI) represents the preferred reperfusion strategy in patients with ST-elevation myocardial infarction (STEMI), because it is more effective than fibrinolysis in reducing cardiovascular events, including death [1,2]. Despite successful coronary artery flow restoration, suboptimal myocardial perfusion occurs in up to 40–70% of STEMI patients depending on the method used, especially among patients with diabetes [3,4]. Over the last decades, the prevalence of diabetes in patients with STEMI significantly

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increased and mortality rates remain about 1.5-fold higher in patients with diabetes compared with those without [5]. Antiplatelet therapy with glycoprotein IIb/IIIa receptor inhibitors represents a well-known pharmacological strategy in order to improve microvascular reperfusion in patients undergoing primary PCI [6,7]. Randomized studies and meta-analyses reported a mortality reduction in diabetic patients with STEMI receiving intravenous administration of abciximab [8], a chimeric monoclonal antibody fragment inhibiting the platelet bound glycoprotein IIb/IIIa receptor. However, experimental data suggested additional antiplatelet, antithrombotic and anti-inflammatory effects when high local abciximab concentrations are reached [9], Therefore, we performed a pooled analysis of randomized studies to assess reperfusional and clinical outcomes after intracoronary compared with intravenous bolus abciximab administration in diabetic patients undergoing primary PCI.

2. Methods

Our population is represented by a total of 3158 patients enrolled in 5 randomized trials [10–14]. Detailed data have previously been published and the main characteristic of each study are summarized in the Table 1 [15]. Briefly, all STEMI patients were admitted within 12 h from symptom onset and received dual antiplatelet therapy with aspirin and clopidogrel (300–600 mg) or prasugrel (60 mg) loading dose. Peri-procedural anticoagulation consisted of intravenous unfractioned heparin in all cases. Patients were randomized to receive intracoronary (n = 1590 or 50.43%) or intravenous (n = 1568 or 49.7%) bolus abciximab at the time of primary PCI. In patients randomized to the intracoronary route, abciximab bolus was administered through the guiding catheter. Diabetes was defined as known diabetes at admission. Reperfusional endpoints were: post-procedural Thrombolysis in Myocardial Infarction Study (TIMI) flow grade 3, myocardial blush grade (MBG) 3 and complete (>70%) ST-segment resolution at 60–90 min. The primary clinical endpoint was the composite of death or reinfarction. Secondary endpoints were the individual endpoints: death, reinfarction and definite or probable stent thrombosis, according to Academic Research Consortium criteria [16]. All clinical endpoints were evaluated at 30-day follow-up and managed according to the intention-to-treat principle.

Table 1
Main characteristics of included trials.

Trial	Number of patients enrolled	Study design	Primary endpoint	Main exclusion criteria	Abciximab doses	Intracoronary abciximab administration method	Period of enrollment
AIDA STEMI [14]	IC (n = 1032) vs. IV (n = 1033)	Multi-center	All-cause death, reinfarction, new congestive heart failure at 90 days	Rescue PCI, ischemic time >12 h	Bolus (0.25 mg/kg body weight) followed by 12-hour infusion (0.125 μg/kg/min)	Through the guiding catheter after infarct-related artery recanalization by PCI wire before balloon dilatation	2008–2011
CICERO [11]	IC (n = 271) vs. IV (n = 263)	Single-center	Complete ST-segment resolution	Rescue PCI, cardiogenic shock, ischemic time >12 h	Bolus only (0.25 mg/kg body weight)	Through the guiding catheter proximal to the lesion after thrombectomy	2008–2010
Dominguez-Rodriguez et al. [10]	IC (n = 25) vs. IV (n = 25)	Single-center	Soluble CD40 ligand levels	Rescue PCI, cardiogenic shock, ischemic time >6 h	Bolus (0.25 mg/kg body weight) followed by 12-hour infusion (0.125 μg/kg/min)	Through the guiding catheter after thrombectomy	2008
Iversen et al. [12]	IC (n = 185) vs. IV (n = 170)	Single-center	Death, target-vessel revascularization, reinfarction at 30 days	Ischemic time >12 h	Bolus (0.25 mg/kg body weight) followed by 12-hour infusion (0.125 μg/kg/min)	Through the guiding catheter after infarct-related artery recanalization by PCI wire before balloon dilatation	2006–2008
Thiele et al. [13]	IC (n = 77) vs. IV (n = 77)	Single-center	Infarct size and microvascular obstruction at MRI	Rescue PCI, cardiogenic shock, ischemic time >12 h	Bolus (0.25 mg/kg body weight) followed by 12-hour infusion (0.125 μg/kg/min)	Through the guiding catheter after infarct-related artery recanalization by PCI wire before balloon dilatation	2006

AIDA STEMI = abciximab intracoronary versus intravenously drug application in ST-elevation myocardial infarction. CICERO = comparison of intracoronary versus intravenous abciximab administration during emergency reperfusion of ST-segment elevation myocardial infarction trial. PCI = percutaneous coronary intervention. IC = intracoronary. IV = intravenous.

Table 2
Baseline characteristics by diabetic status.

	Subjects with DM (n = 584)	Subjects without DM (n = 2574)	p
Age, yrs	66.8 ± 12	61.8 ± 12	<0.001
Male, n (%)	387 (66.3)	2008 (78)	<0.001
Hypertension, n (%)	484 (82.9)	1434 (55.7)	<0.001
Dyslipidemia, n (%)	322 (55.1)	871 (33.8)	<0.001
Current smoker, n (%)	188 (32.2)	1181 (45.9)	<0.001
Family CAD history, n (%)	171 (29.3)	835 (33.1)	0.07
Previous MI, n (%)	83 (14.2)	238 (9.2)	<0.001
Previous revascularization, n (%)	98 (16.8)	250 (9.7)	<0.001
Thrombectomy, n (%)	162 (27.7)	806 (31.3)	0.09
Anterior MI, n (%)	278 (47.6)	1161 (45.1)	0.27
Diseased vessel, n (%)		<0.001	
1	232 (39.7)	1276 (51.1)	
2	178 (30.5)	705 (28.2)	
3	174 (29.8)	517 (16.8)	
Infarct-related vessel, n (%)		0.04	
No infarct-related artery	0	2 (0.1)	
Left anterior descending	256 (43.9)	1125 (45.1)	
Left circumflex	79 (13.6)	300 (12)	
Right coronary	237 (40.7)	1052 (42.2)	
Left main	7 (1.2)	13 (0.5)	
Saphenous-vein graft	4 (0.7)	3 (0.1)	
Prasugrel use, n (%)	33 (5.7%)	162 (6.3%)	0.63

DM: diabetes mellitus; CAD: coronary artery disease; MI: myocardial infarction.