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Eptifibatide Is Noninferior to Abciximab in Primary Percutaneous Coronary Intervention

Results From the SCAAR (Swedish Coronary Angiography and Angioplasty Registry)

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Objectives The aim of this study was to test the noninferiority of eptifibatide relative to abciximab in patients with ST-segment elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention (PCI).

Background Glycoprotein IIb/IIIa inhibitors are recommended by international guidelines in patients with acute coronary syndromes undergoing PCI. Abciximab is recommended with a higher level of evidence than eptifibatide in patients with STEMI. No large, prospective, randomized trial comparing abciximab and eptifibatide has been published.

Methods All (n = 11,479) STEMI patients in Sweden who underwent primary PCI and received either eptifibatide or abciximab from 2004 to 2007 were derived from the SCAAR (Swedish Coronary Angiography and Angioplasty Registry). The primary end point was death or myocardial infarction (MI) during 1-year follow-up, with adjustment for baseline differences with a multivariate logistic regression analysis including propensity score. The pre-specified noninferiority margin was set to 1.29.

Results The combined end point occurred in 353 of 2,355 patients (15.0%) treated with eptifibatide and in 1,432 of 9,124 patients (15.7%) treated with abciximab. The unadjusted odds ratio (OR) for eptifibatide versus abciximab was 0.95 (95% confidence interval [CI]: 0.84 to 1.08). Multivariate adjustment (n = 11,317) confirmed noninferiority, with an OR of 0.94 (95% CI: 0.82 to 1.09). The adjusted secondary end points of death and MI separately also showed noninferiority, with ORs of 0.99 (95% CI: 0.82 to 1.19) and 0.88 (95% CI: 0.73 to 1.05), respectively.

Conclusions This large registry study suggests that eptifibatide is noninferior to abciximab in patients with STEMI undergoing primary PCI with respect to death or MI during 1 year, thereby supporting the use of either drug in clinical practice. (J Am Coll Cardiol 2010;56:470–5) © 2010 by the American College of Cardiology Foundation

Glycoprotein (GP) IIb/IIIa inhibitors potently inhibit platelet aggregation and reduce the incidence of ischemic events in patients undergoing percutaneous coronary interventions (PCIs), especially in patients with acute coronary syndromes (ACS) (1–4). Abciximab is recommended with a high level of evidence in both the European and American guidelines as adjunctive treatment during PCI for high-risk patients with ACS, including primary PCI in patients with ST-segment elevation myocardial infarction (STEMI) (5–8). Eptifibatide and tirofiban have less scientific documentation but are approved for adjunctive medical therapy during PCI in stable coronary disease, as well as in patients with ACS (2,4,7,8). Eptifibatide is not recommended for primary PCI by the European guidelines (5) and receives a lower level of evidence compared with abciximab in the latest updated American College of Cardiology/American Heart Association STEMI guidelines (6,9).

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In 2004, 2 large Swedish university hospitals changed their GP IIb/IIIa inhibitor therapy from abciximab to

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eptifibatide on all indications to reduce pharmacological costs. An additional 7 hospitals (of 27 hospitals performing PCI) have been using both abciximab and eptifibatide (10). The present study was designed to test a pre-specified hypothesis that eptifibatide is noninferior to abciximab with respect to death or myocardial infarction (MI) during 1 year in patients with STEMI undergoing primary PCI.

Methods

Subjects and study design. The patient population was derived from SCAAR (Swedish Coronary Angiography and Angioplasty Registry), a registry with complete coverage of all hospitals performing coronary angiography and interventions in Sweden. The registry is supported by Swedish Health Authorities and is independent of commercial funding (10).

Between January 2004 and December 2007, a total of 15,542 procedures were performed in 15,120 patients with STEMI as primary PCI. In this retrospective observational study, only patients with primary PCI receiving adjunctive therapy with either eptifibatide or abciximab were included (n = 11,479) (10). Each patient was followed for 1 year and was included in the study only once. In hospitals using both eptifibatide and abciximab, the selection of the GP IIb/IIIa inhibitor was at the operator's discretion. Patients receiving tirofiban (n = 463) were excluded as well as patients undergoing rescue PCI. Patients treated with adjunctive fondaparinux (n = 15) or bivalirudin (n = 63) were not excluded. All episodes of PCI-related bleeding during the hospital stay were to be reported in the SCAAR registry (10), but this assessment was not a part of the primary objective of the study.

The long-term follow-up was derived by merging the SCAAR database with the Swedish Cause of Death Register and the Swedish National Patient Register regarding reinfarction after hospital discharge (International Classification of Diseases-10th Revision codes I21 and I22). The study was approved by the local ethics committee at Uppsala University. The study complied with the Declaration of Helsinki.

Statistical analysis. The primary hypothesis was that eptifibatide would be noninferior to abciximab with respect to the primary end point of death or MI at 1 year. The pre-specified noninferiority margin was set to 1.29, preserving 50% of the estimated effect by abciximab by the point estimate of the odds ratio (OR) of abciximab versus placebo in patients with STEMI (11,12). The pre-specified secondary end points were death and MI separately during 1 year of follow-up.

Logistic regression with drug as a predictor was used to obtain the estimates of ORs and 95% confidence intervals (CIs). To compensate for pre-treatment differences, we added propensity score (13) as a predictor in a multivariate logistic regression. The individual propensity scores, defined as the conditional probability of obtaining eptifibatide, based on all variables in Tables 1 and 2, were estimated using multivariate logistic regression. Age was dichotomized (≤65 years vs. >65 years) before entering the model. Fondaparinux and bivalirudin were not used as individual factors in the propensity score analysis.

Abbreviations and Acronyms

ACS = acute coronary syndromes
CI = confidence interval
GP = glycoprotein
MI = myocardial infarction
OR = odds ratio
PCI = percutaneous coronary intervention
STEMI = ST-segment elevation myocardial infarction

Results

A total of 11,479 patients with STEMI underwent primary PCI with adjunctive therapy of either eptifibatide (n = 2,355) or abciximab (n = 9,124). Baseline characteristics are presented in Table 1, and ongoing or periprocedural medications are listed in Table 2.

Table 1 Clinical Characteristics

Variable	All Patients (n = 11,479)	Abciximab (n = 9,124)	Eptifibatide (n = 2,355)
Age, yrs	11,479	65 (57–74)	65 (57–74)
Women	11,479	28.1% (2,568)	27.0% (636)
Diabetes	11,479	17.7% (1,616)	16.3% (385)
Hypertension	11,479	34.6% (3,157)	33.6% (791)
Hyperlipidemia	11,478	18.1% (1,647)	16.5% (389)
Congestive heart failure	11,479	3.3% (300)	2.9% (69)
Current smoker	11,476	29.5% (2,688)	27.7% (652)
Previous myocardial infarction	11,479	14.9% (1,355)	14.8% (349)
Previous PCI	11,465	8.6% (782)	9.0% (211)
Previous CABG	11,475	2.7% (242)	3.0% (71)
Previous stroke	11,479	5.0% (458)	4.1% (97)
Previous renal failure	11,479	1.0% (88)	1.2% (28)
Previous major bleeding	11,479	3.2% (291)	2.6% (62)

Data are expressed as median (25th–75th percentile) or percent (frequency).
CABG = coronary artery bypass grafting; n = number of patients with nonmissing values; PCI = percutaneous coronary intervention.