Original Article

# Immediate outcomes of eptifibatide therapy during intracoronary stent implantation

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## Abstract

**Background:** The objective of the present study was to assess the major immediate outcomes of eptifibatide therapy during intracoronary stent implantation.

**Materials and Methods:** In an interventional study, patients undergoing percutaneous coronary intervention (PCI) were randomized into either the eptifibatide ($n = 100$) or the control ($n = 107$) group. In each group, demographic and clinical characteristics such as cardiac death, stent thrombosis (ST), myocardial infarction (MI), rates of target lesion and vessel revascularization, cerebral vascular accident (CVA), and emergency coronary artery bypass grafting (CABG) were recorded.

**Results:** The overall rates of major adverse events such as mortality, Stent thrombosis (ST), Myocardial Infarction (MI), target lesion revascularization (TLR), target vessel revascularization (TVR), CVA, and emergency CABG within 24 h after stent implantation were low and comparable between the two groups; $P > 0.05$ considered significant for all comparisons.

**Conclusion:** There were no statistical differences between the clinical outcomes of groups administered with single-dose intracoronary eptifibatide and control groups among patients undergoing PCI during stent implantation.

**Key Words:** Eptifibatide, immediate clinical outcome, percutaneous coronary intervention, stent implantation

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## INTRODUCTION

Coronary heart disease (CHD) is the narrowing or blockage of the coronary arteries generally caused by atherosclerosis.[1] The outreach of stents has been a notable progress in the treatment of obstructive coronary artery disease (CAD) since the introduction of balloon angioplasty.[2] Significant reduction in outcomes of mortality, myocardial infarction (MI), and target vessel revascularization (TVR) using parenteral glycoprotein IIb/IIIa receptor antagonists has been widely reported for patients with acute coronary syndrome.[3-6] Glycoprotein IIb/IIIa receptor antagonists consist of: The monoclonal antibody abciximab, the peptide receptor antagonist eptifibatide, and the nonpeptide receptor antagonists tirofiban and lamifiban.[7] Among them eptifibatide (Integrilin) is often less expensive and more widely available in many hospitals.[8,9]

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Eptifibatide has been shown to ameliorate cardiac outcomes in patients with percutaneous coronary intervention (PCI) by lessening the incidence of major adverse cardiac events.[10-12] In an investigation, the complementary effect of thienopyridine pretreatment and the integrin blockade in coronary stent intervention were assessed; according to their results, pretreatment with thienopyridine decreased the rate of ischemic complications regardless of eptifibatide treatment. They expressed that the efficacy of eptifibatide is dependant on the presence of a loading dose of thienopyridine administration. Also, optimal outcomes were attained by receiving thienopyridine pretreatment along with eptifibatide therapy.[13] In a study conducted between January 2003 and August 2005, the long-term mortality after bolus-only administration of abciximab, eptifibatide, and tirofiban during PCI were evaluated. As is shown in their results, eptifibatide was able to ameliorate long-term survival prognosis compared to abciximab when applied bolus-only.[14] O'Shea *et al*. in a randomized controlled trial (RCT) entitled "Platelet glycoprotein IIb/IIIa Integrin blockade with Eptifibatide in coronary stent intervention" showed that adjunctive eptifibatide therapy during coronary stent implantation is beneficial within a 6-month follow-up.[15] Intracoronary Eptifibatide bolus administration during PCI in patients with acute coronary syndromes indicated a higher local platelet glycoprotein IIb/IIIa receptor occupancy, which is related to improved microvascular perfusion demonstrated by improving the corrected thrombolysis in the MI frame count.[16] In an investigation, different outcomes concerning the use of eptifibatide instead of abciximab in patients undergoing primary PCI were assessed. There were no differences expressed in the early outcomes of patients treated with eptifibatide, compared to patients treated with abciximab.[8] Also, in another survey the clinical outcomes of eptifibatide and abciximab in acute ST elevation MI (STEMI) patients undergoing PCI were compared; no significant differences were observed in clinical outcomes between STEMI patients treated with eptifibatide or abciximab. It has been suggested that because of the lower cost of eptifibatide, it can be a suitable substitute for abciximab and reduce the overall medication costs while maintaining beneficial safety and efficacy.[17] Although eptifibatide has been fairly studied in patients with CAD, there are few available data in the case of a single dose (10 cc) injection prior to coronary stent implantation to justify its use in PCI. The objective of the present study was to evaluate the effect of eptifibatide before intracoronary stent implantation on immediate outcomes in patients with CAD in a double-blind RCT.

## MATERIALS AND METHODS

The design of this study was a single-center, double-blind RCT comparing eptifibatide plus stenting with stenting alone in 207 patients during intracoronary stent implantation.

The study was conducted between January and December 2012 and performed in an educational hospital (Shahid-Chamran hospital, Isfahan, Iran). The intervention protocol was approved by the Ethics Committee of the Isfahan University of Medical Sciences, and all patients provided written informed consent. The nonprobability consecutive sampling method was used.

All patients were randomly divided into one of the two groups by Random Allocation Software (SPSS Inc. Chicago).[18] According to the randomization protocol, eptifibatide (150 μg/kg) was administered in 107 patients just before the stenting procedure.

The inclusion criteria were: Age 30-75 years, stable or unstable angina and/or documentation of myocardial ischemia attributable to coronary artery stenosis, patients without renal failure (renal failure defined as a serum creatinine ≥2 mg/dl), and patients without any infectious or systemic disease.

It was decided that cardiac death, stent thrombosis (ST), MI, rates of target lesion and vessel revascularization, cerebral vascular accident (CVA), and emergency CABG would be the major endpoints of the present study.

MI will be distinguished as Q wave or non-Q wave (defined as elevation of total creatine kinase [CK] two times above the upper limit of normal with a positive MB fraction in the absence of pathological Q waves).[19] Target lesion revascularization (TLR) is defined as any revascularization performed on the treated segment and target vessel revascularization (TVR) as any percutaneous reintervention performed on the treated vessel.[20] Urgent or emergency CABG is defined as a surgical procedure immediately following catheterization, mandated by clinical circumstances.[21] Acute coronary ST, defined as ST within 30 days of deployment, has been reduced to <1-2% as a result of improved deployment techniques that fully appose stent to the vessel wall and the use of antiplatelet agents.[22]

All data were analyzed using PASW 18.0 (SPSS Inc., Chicago, IL, USA). Data are presented as Mean ± SD for continuous variables and number (percent) for categorical ones.

We used the Kolmogorov-Smirnov test for normality in order to evaluate the assumption of *t*-test. Statistical differences between studied groups were assessed by the independent-samples *t*-test, the Chi-square test, and Fisher's exact test. $P < 0.05$ denoted statistical significance.

## RESULTS

The flow-diagram of the study is shown in Figure 1. A total of 110 males (53.1%) and 97 females (46.9%) were included in the analysis. The mean age of the participants was 61.1 ± 8.6 years (range, 45-87 years), and there were no significant statistical differences in age and sex distributions between the two groups ($P = 0.81$ and $P = 0.97$, respectively). The demographic and clinical characteristics of the study population categorized by groups are shown in detail in Table 1.

As is shown in the table, the frequency of smoking, hypertension, family history of CAD, prior MI, and hyperlipidemia were not statistically significant ($P > 0.05$).

The frequency of diabetes mellitus (DM) in the case group was significantly higher than that in the controls (42% vs. 21.5%; $P = 0.001$).

In this study we did not find any significant to statistical differences between the eptifibatide group and the control group in clinical outcomes such as cardiac and noncardiac death, ST, MI, TLR, TVR, CVA, and emergency CABG ($P > 0.05$).

## DISCUSSION

Our study examined the clinical immediate outcomes in a consecutive series of patients with CAD who underwent primary PCI and received eptifibatide plus stenting, or stenting alone as a control group, in a double-blind RCT.

The principal finding of the present investigation is that in the studied population of patients with CAD, single-dose intracoronary eptifibatide plus stenting result in similar clinical outcomes when compared to stenting alone.

In accordance with our findings, Raveendran *et al*. in an observational analysis conducted between January 1999 and January 2004 compared the clinical outcomes of 576 patients treated with eptifibatide ($n = 249$) or abciximab ($n = 327$) during primary PCI. As they noted, there were no significant differences between the outcomes of in-hospital death or MI in both eptifibatide- and abciximab-treated groups. They also remarked that eptifibatide was useful and safe as adjunctive pharmacotherapy for patients undergoing primary PCI for acute MI in comparison with abciximab.[3] In an investigation done between October 2002 and July 2006, different outcomes of 3,541 patients concerning the use of eptifibatide ($n = 2,812$) instead of abciximab ($n = 729$) undergoing primary PCI were assessed. As their results indicated, there were no significant differences in case of early outcomes of patients treated with eptifibatide compared with patients treated with

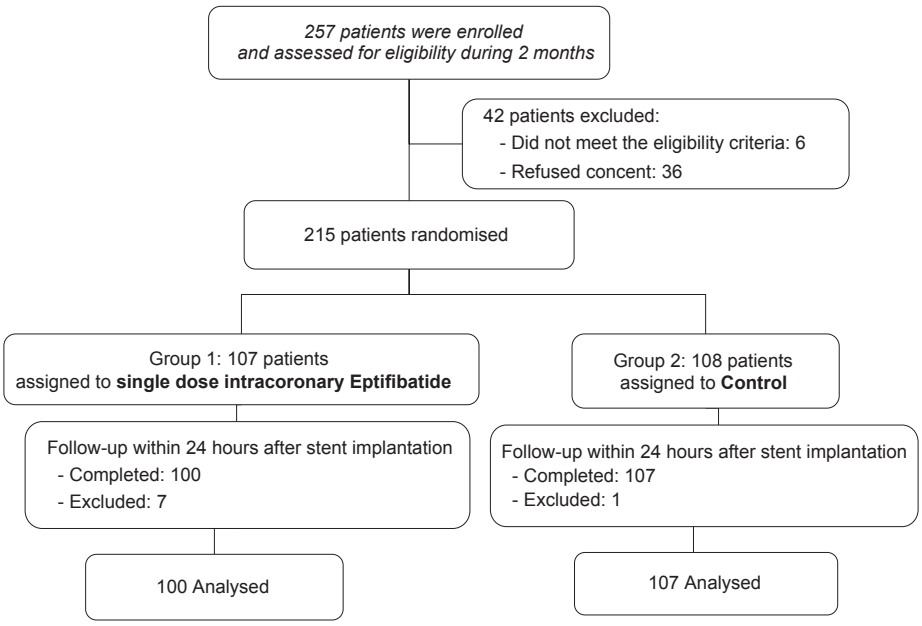


**Figure 1:** Flow diagram of the study

**Table 1: Demographic features and immediate clinical outcomes of 207 patients divided by studied groups**

| Characteristics | Groups | | *P* |
|---|---|---|---|
| | Eptifibatide (*n*=100) | Control (*n*=107) | |
| Age (years) | 67.2±7.9 | 66.9±9.2 | 0.81 |
| Gender (male/female) | 47/53 | 50/57 | 0.97 |
| History of smoking | 32 (32) | 28 (26.2) | 0.36 |
| DM | 24 (42) | 23 (21.5) | 0.001 |
| HTN | 34 (34) | 24 (22.4) | 0.064 |
| Family history of CAD | 23 (23) | 14 (13.1) | 0.063 |
| Prior MI | 11 (11) | 10 (9.3) | 0.694 |
| HLP | 21 (21) | 21 (19.6) | 0.806 |
| Vessel place | | | 0.018 |
| LAD /LCX /RCA | 44/19/37 | 68/14/25 | |
| Mortality | | | 0.684 |
| Cardiac death | 0 | 2 (1.9) | |
| Noncardiac death | 2 (2) | 2 (1.9) | |
| ST | 1 (1) | 2 (1.9) | 0.601 |
| MI | 2 (2) | 1 (0.9) | 0.522 |
| TLR | 1 (1) | 2 (1.9) | 0.601 |
| TVR | 2 (2) | 1 (0.9) | 0.522 |
| CVA | 1 (1) | 5 (4.7) | 0.115 |
| Emergency CABG | 0 | 0 | - |

DM: Diabetes mellitus, HTN: Hypertension, CAD: Coronary artery disease, MI: Myocardial infarction, HLP: Hyperlipidemia, LAD: Left anterior descending coronary artery, LCX: Left circumflex coronary artery, RCA: Right coronary artery, ST: Stent thrombosis, TLR: Target lesion revascularization, TVR: Target vessel revascularization, CVA: Cerebral vascular accident, CABG: Coronary artery bypass grafting. Data are expressed as Mean±SD, number and number (percent). *P* values calculated by independent-sample *t*-test, chi-square test, and Fisher's exact test

abciximab.[8] Also, in a study published in 2002 by Stone *et al*., upon 2,082 patients with acute MI and in a comparison of angioplasty with stenting, with or without abciximab, no significant differences were observed between the percutaneous transluminal coronary angioplasty plus abciximab, stenting alone, or stenting plus abciximab cohorts at 30 days follow-up.[23] The incorporation of the results given by Stone *et al*. and reports that indicated similar outcomes for eptifibatide and abciximab could be a confirmation of our findings.

The Enhanced Suppression of the Platelet IIb/IIIa Receptor with Integrilin Therapy (ESPRIT) indicated the efficacy of adjunctive eptifibatide therapy during coronary stent implantation at 48 h and at 30 days follow-up. Secondary studies proved the benefits of eptifibatide upon composite rates of death or MI and death, infarction, or TVR during 6 and 12 months follow-up.[11,15,24]

Although several studies have shown obvious reduction in a variety of ischemic events in patients, which results from receiving eptifibatide as adjunctive pharmacotherapy during PCI,[25,26] in our results we could not find any significant differences concerning the effect of eptifibatide upon clinical outcomes compared with the control group. The failure to reach any statistical significance between the two groups (eptifibatide and control), despite the differences reported by former studies, may be related to the small sample size, which greatly reduced the power of the statistical analyses, or to the relatively short time of follow-up. Some supplementary studies with larger sample sizes and more follow-up time are needed to evaluate the real effect of eptifibatide on clinical outcomes.

## CONCLUSION

We could not find any significant statistical differences between the short-term clinical outcomes of the single-dose intracoronary eptifibatide and control groups in patients undergoing primary PCI during stent implantation. On the other hand, the use of eptifibatide before intracoronary stent implantation did not have any positive effect on immediate outcomes in patients with CAD.

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### Conflicts of interest

There are no conflicts of interest.

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