Original Article

Evaluation of the Rational use of Eptifibatide among Patients with Acute Coronary Syndrome Referred to Shahid Chamran Heart Hospital

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ABSTRACT

Objective: This cross-sectional descriptive study was conducted over 3 months (April–June 2025) among acute coronary syndrome (ACS) patients who received eptifibatide at Shahid Chamran Hospital, Isfahan. **Methods:** Patient demographics, diagnosis, and the chosen therapeutic approach (revascularization or ischemia-guided) were collected. Data on concomitant medications (including aspirin and P2Y12 inhibitors), timing, and dosing were extracted from medical records. Details on eptifibatide administration (total dose and time) were captured. The procedural time and intra-procedural events (thrombotic events, no-reflow) were documented. The appropriateness of eptifibatide use was evaluated against European Society of Cardiology-ACS 2023 and American Heart Association-ACS 2025 guidelines. **Findings:** A total of 150 patient records were reviewed. Only 48% of eptifibatide prescriptions were guideline-concordant. Of the rational prescriptions, two cases were due to intra-procedural thrombotic events, five due to no-reflow phenomena, and 65 due to insufficient time for the P2Y12 inhibitor to achieve a therapeutic effect (all received clopidogrel as the P2Y12 inhibitor) at percutaneous coronary intervention. Notably, 97.33% of patients received clopidogrel, while only 2.66% received ticagrelor, the faster-onset P2Y12 inhibitor preferred by guidelines over clopidogrel. This suggests that using ticagrelor instead of clopidogrel in these cases might have eliminated the need for eptifibatide owing to its quicker onset. **Conclusion:** The study shows limited concordance between eptifibatide prescribing and guidelines. In addition, using ticagrelor instead of clopidogrel might eliminate the need for eptifibatide owing to its quicker onset.

Keywords: *Acute coronary syndrome, eptifibatide, GP IIb/IIIa inhibitor*

Introduction

Acute coronary syndrome (ACS) remains one of the leading causes of mortality worldwide.[1] The principal mechanism underlying ACS is rupture of an unstable atherosclerotic plaque with subsequent occlusive thrombus formation in the coronary arteries. Exposure of the subendothelial matrix to circulating platelets during plaque rupture initiates a platelet signaling cascade. Consequently, incorporating antiplatelet agents is a cornerstone of ACS management. Generally, antiplatelet therapies used in ACS have included aspirin plus a P2Y12 receptor inhibitor (ADP P2Y12 receptor antagonist) with or without a GP IIb/IIIa inhibitor.[2,3]

In the past decade, GP IIb/IIIa inhibitors were widely used in patients with ACS undergoing percutaneous coronary intervention (PCI). However, more recent evidence has not demonstrated a clear advantage of GP IIb/IIIa inhibitors in ACS when compared with no use, given the emergence of antiplatelet agents with greater potency and faster onset of action. With the advent of newer P2Y12 inhibitor agents such as ticagrelor and

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prasugrel, which offer faster onset (approximately 15–30 min) and markedly greater potency than clopidogrel, these agents have increasingly become first-line therapies for ACS. Consequently, guidelines have de-emphasized routine use of GP IIb/IIIa inhibitors, limiting their use to scenarios such as insufficient response to P2Y12 inhibitors, thrombotic events during angioplasty, or no-reflow phenomena. Nevertheless, despite guideline recommendations, GP IIb/IIIa inhibitors continue to be prescribed in ACS.[4,5]

The aim of this study was to evaluate the rational use of eptifibatide in light of recently updated guideline recommendations at Chamran Heart Hospital.

Methods

This was a cross-sectional descriptive study conducted over 3 months (April, May, and June 2025) among patients receiving eptifibatide at Shahid Chamran Hospital in Isfahan, affiliated to Isfahan University of Medical Sciences. The study was approved by the Research Ethics Committees of the Schools of Pharmacy and Nutrition, Isfahan University of Medical Science. (Ethical Code: IR.MUI.PHANUT.REC.1402.102).

Inclusion criteria were defined as receipt of at least one vial of eptifibatide during the 3-month study period. Exclusion criteria included incomplete medical records or a lack of accessible required information, which led to exclusion from the study.

All patients received guideline-recommended ACS medications, including aspirin, a P2Y12 inhibitor, an anticoagulant (heparin or enoxaparin), and a statin. Patient demographics (age and sex), diagnosis, and the chosen therapeutic approach (revascularization or ischemia-guided) were collected. Data on concomitant medications, including antiplatelets (e.g. aspirin and P2Y12 inhibitor), as well as the exact timing and dosing of these medications, were extracted from medical records. Details on eptifibatide administration (including total dose and exact time of administration) were captured. The precise time of the procedure and intra-procedural events – such as thrombotic events, or no-reflow phenomena – were documented from operative notes and case records.

The most up-to-date guidelines regarding the use of GP IIb/IIIa inhibitors are the European Society of Cardiology-ACS (ESC-ACS) 2023 and American Heart Association-ACS 2025 guidelines.[6,7] According to the recommendations of these two guidelines, the following scenarios are considered logical indications for eptifibatide administration:

- In the presence of thrombotic events during angioplasty or no-reflow phenomena
- In situations where the efficacy of P2Y12 inhibitors during angioplasty cannot be assured:
  - In this study, the following scenario was considered equivalent to this criterion: insufficient time for the P2Y12 inhibitor to achieve a therapeutic effect at the time of PCI, 120 min for clopidogrel, with a 600 mg loading dose. Given the rapid onset of ticagrelor and prasugrel, the time interval need not be considered, and there is no indication for using eptifibatide unless a thromboembolic event or no-reflow occurs during angioplasty.[6-8]

The appropriateness of eptifibatide administration was evaluated in terms of dosing and indication (based on the guideline recommendation), with the findings reported as a percentage.

Results

A total of 150 patient records (110 men and 40 women) who presented to Shahid Chamran Hospital within the 3 months were reviewed. The mean age of the participants was 60.8 years. Regarding the diagnosis, 60% (90 patients) and 40% (60 patients) were NSTE-ACS and STE-ACS, respectively. One hundred forty-six patients received clopidogrel, while only four patients received ticagrelor as the P2Y12 inhibitor [Table 1].

As shown in Table 2, only 48% of eptifibatide prescriptions were guideline concordant. Of the 48% deemed rational, two cases were due to thrombotic events during the procedure, five cases were attributed to no-reflow phenomena, and 65 cases were due to insufficient time for the P2Y12 inhibitor (all 65 cases received clopidogrel) to achieve therapeutic effect at the time of PCI. In other words, these 65 clopidogrel-treated patients had a time interval of <120 min between the P2Y12 administration and PCI.

As shown in Table 2, 65 patients (44/33%) deemed to require eptifibatide due to insufficient time for the

Table 1: Demographic characteristics of the included patients

Total number of patients studied	*n* (%)
Gender	
Male patients	110 (73.3)
Female patients	40 (26.6)
Diagnosis	
STE-ACS	68 (40)
NSTE-ACS	82 (60)

STE-ACS=ST-elevation acute coronary syndrome, NSTE-ACS=Non-STE-ACS

Table 2: Rational and irrational use of eptifibatide categorized by the indication and the type of the prescribed P2Y12 inhibitor agent

Rational/irrational indications	P2Y12 inhibitor agent	Reason for use	*n* (%)
Rational eptifibatide use (*n*=72; 48%)	Clopidogrel	Insufficient time interval between the administration of P2Y12 inhibitor and eptifibatide (time interval<120 min)	65 (90.27)
		Thrombotic events during the procedure	2 (2.77)
		No flow	5 (6.94)
	Ticagrelor	-	0
Irrational eptifibatide use (*n*=78; 52%)	Clopidogrel	-	74 (94.87)
	Ticagrelor	-	4 (5.12)

P2Y12 inhibitor to achieve a therapeutic effect at the time of PCI were those who received clopidogrel, with the interval between clopidogrel administration and PCI <120 min. This suggests that using ticagrelor instead of clopidogrel in these cases might have eliminated the need for eptifibatide owing to its faster onset. It is worth mentioning that in this study, only 4 patients received ticagrelor, the P2Y12 inhibitor preferred over clopidogrel by guideline recommendations.

In addition, only 33/45 (73.3%) of patients received both the bolus and infusion dosing in accordance with the guidelines, and others just received the bolus dose.

Discussion

This study was designed to evaluate the rational use of eptifibatide in light of recently updated guideline recommendations at Chamran Heart Hospital. The findings of this study indicate a low level of concordance between eptifibatide prescribing and the relevant guidelines.

Irrational drug use represents one of the most significant challenges in modern healthcare systems. Rational medication use is guided by evidence-based guidelines and tailored to patients' clinical needs.[9] This study is a Medication Use Evaluation (MUE), a performance-improvement method that focuses on evaluating and improving medication-use processes with the goal of optimal patient outcomes. The MUE system assesses actual prescribing patterns, including appropriate indications, drug selection, and dosage. According to ASHP (American Society of Health-System Pharmacists) recommendations,[10] medications possessing any of the following characteristics may be selected as subjects for MUE studies:

1. High cost and/or scarcity
2. Recent changes in guidelines related to drug prescribing indications
3. Reports indicating an unexpected increase in drug utilization within the hospital
4. Presence of adverse drug reactions and medication errors.

Eptifibatide was selected for this study due to recent guideline changes regarding its administration (ESC-ACS 2023 and AHA 2025 guidelines), which are based on new clinical evidence, as well as its high cost. Eptifibatide is a cyclic heptapeptide and a potent glycoprotein IIb/IIIa receptor antagonist classified among the parenteral antiplatelet agents.[6,7] In ACS, exposure of the subendothelial matrix to circulating platelets during plaque rupture initiates a platelet signaling cascade, activating the GP IIb/IIIa receptor and promoting cross-linking of platelets by fibrinogen to form a stable platelet aggregate. GP IIb/IIIa inhibitors, such as eptifibatide, prevent receptor activation and thereby hinder platelet aggregation.[2,3]

In the past decade, GP IIb/IIIa inhibitors were recommended to use in patients with ACS undergoing PCI. Studies from that era suggested a potential mortality benefit in acute myocardial infarction; However, these studies were largely conducted before the advent of newer, more potent, and rapidly acting P2Y12 inhibitors such as ticagrelor and prasugrel.[11] More recent evidence has not demonstrated a clear advantage of GP IIb/IIIa inhibitors in ACS when compared with no use, given the emergence of P2Y12 inhibitor agents with greater potency and faster onset of action.[12] New P2Y12inhibitor agents such as ticagrelor and prasugrel, which offer faster onset (approximately 15–30 min) and markedly greater potency than clopidogrel, have increasingly become first-line therapies for ACS.[13] Consequently, guidelines have de-emphasized routine use of GP IIb/IIIa inhibitors when potent P2Y12 inhibitors are used and limited their use to scenarios such as insufficient response to P2Y12 inhibitors, thrombotic events during angioplasty, or no-reflow phenomena.[14] Given that ticagrelor is the preferred P2Y12 inhibitor in ACS patients undergoing PCI, ESC and AHA do not recommend routine GP IIb/IIIa inhibitor use because of no proven ischemic benefit and higher bleeding risk. There is, however, no explicit recommendation regarding adjunctive use of these agents with clopidogrel.[6,7]

In this study, we found that the main reason for prescribing eptifibatide was the use of clopidogrel instead

of the more potent P2Y12 inhibitors such as ticagrelor and prasugrel. Studies have shown that a 600 mg loading dose of clopidogrel typically begins antiplatelet activity after about 2 h, whereas a 180 mg loading dose of ticagrelor achieves this in roughly 15–30 min. Given that many patients with ACS require urgent intervention, ideally within 120 min of admission for patients with STEMI, the time to achieve adequate platelet inhibition is critical.[5] Theoretically, PCI performed within <2 h after clopidogrel administration cannot guarantee sufficient antiplatelet inhibition, although studies addressing this issue are lacking. Because ticagrelor has a faster onset of action, it could obviate the need for GP IIb/IIIa inhibitors in many cases.[4,5]

In this study, more than half of the eptifibatide prescriptions were due to inadequate time for the P2Y12 inhibitor effect, with nearly half of these intervals being <120 min. If ticagrelor had been given instead of clopidogrel, its faster onset could have eliminated the need for eptifibatide in these cases. Therefore, ticagrelor, in addition to being more effective and guideline-concordant, has the potential to reduce eptifibatide use.[15] Nevertheless, despite the availability of these agents in the country, clopidogrel remains the preferred choice in many cases at this center. Factors driving continued clopidogrel use include clinicians' extensive experience with clopidogrel, unfamiliarity with newer agents, uncertainty about the brands of new drugs, once-daily dosing with clopidogrel, the higher cost of ticagrelor, and concerns about cost-related nonadherence.[16] It is worth noting that when long-term cost concerns exist for ticagrelor (versus clopidogrel), a de-escalation strategy from a P2Y12 inhibitor commended in the ESC 2023 guideline[7] could be considered: 30 days post-ACS, patients may transition from ticagrelor to clopidogrel for up to 12 months. Additional drivers of high eptifibatide use in this center include limited access to injectable cangrelor, an agent with a rapid onset and short duration of action that, according to guidelines, can substitute for oral P2Y12 inhibitors when there is insufficient time for oral agent effectiveness.[7] This study has several limitations that should be taken into consideration. It is a single-center, cross-sectional study conducted over a short 3-month period and is based on a retrospective review of medical records.

Conclusion

The study shows limited concordance between eptifibatide prescribing and guidelines. The most common reason for use was clopidogrel over ticagrelor, which has a faster onset. If ticagrelor had been used, it could have reduced the need for eptifibatide in these cases.

Authors' Contributions

Javad Amini was the principal investigator of the study. Mehrnoush Dianatkhah participated in preparing the concept and design. Mahnaz Momenzadeh, Ehsan Shirvani, Saeide Bahrani, and Niloufar Mirasi reviewed the manuscript and critically evaluated the intellectual contents. All authors participated in revising the manuscript and preparing the final draft of the manuscript. All authors have read and approved the content of the finalized manuscript and confirmed the accuracy and integrity of any part of the work.

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Conflicts of interest

There are no conflicts of interest.

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