Comparison Between the Effect of Intracoronary Versus Intravenous Eptifibatide on the Outcome of Primary Percutaneous Coronary Intervention to Acute Anterior Myocardial Infarction

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LIST OF ABBREVIATIONS

AMI	Acute myocardial infarction
ACC	American colleague of cardiology
ACCP	American colleague of clinical pharmacy
ACE	Angiotensin converting enzyme
ACEP	American Colleague of Emergency Physicians
ACS	Acute coronary syndrome
ACT	Activated clotting time
AHA	American Heart Association
AIDS	Acquired immune deficiency syndrome
aPPT	Activated partial thromboplastin time
ASA	Acetyl salicylic acid
BP	Blood pressure
CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
CADILLAC	Controlled Abciximab and Device Investigation to Lower Late Angioplasty

	Complications
CAPTIM	Comparison of Angioplasty and Prehospital Thrombolysis in Acute Myocardial Infarction trial
CBC	Complete blood count
CHD	Coronary heart disease
CHF	Congestive heart failure
CK	Creatine kinase
CPB	Cardiopulmonary bypass
CRP	C-reactive protein
CTFCs	Corrected TIMI frame counts
cTnI	Cardiac troponin I
CVA	Cerebrovascular accident
DANAMI	Danish Multicenter Randomized Study on Thrombolytic Therapy versus Acute Coronary Angioplasty in Acute Myocardial Infarction
DIC	Disseminated intravascular coagulopathy
DM	Diabetes mellitus
ECG	Electrocardiogram
ED	Emergency department
ER	Emergency room
ESC	European Society of Cardiology
FBS	Fasting blood sugar
FH	Family history
FTT	Fibrinolytic Therapy Trialists
GP IIb/IIIa	Glycoprotein IIb/IIIa
HDB	High dose bolus
HDL	High density lipoprotein

HIT	Heparin induced thrombocytopenia
hsCRP	High sensitive C-reactive protein
HTN	Hypertension
IABP	Intra-aortic balloon pump
IC	intracoronary
ICH	Intracranial hemorrhage
IHD	Ischemic heart disease
IRA	Infarct related artery
IV	intravenous
LAD	Left anterior descending artery
LBBB	Left bundle branch block
LCA	Left coronary artery
LCX	Left circumflex artery
LDL	Low density lipoprotein
LM	Left main
LMWH	Low molecular weight heparin
LV	Left ventricle
LVEF	Left ventricular ejection fraction
MACE	Major adverse cardiovascular events
MBG	Myocardial blush grade
MCE	Myocardial contrast echocardiography
NRMI	National registry of myocardial infarction
NSAIDS	Non-steroidal anti-inflammatory drugs
NSTEMI	Non-ST segment elevation myocardial infarction
№	Number
P	Probability of chance (significance)

PCI	Percutaneous coronary intervention
PFA	Platelet function test
PTCA	Percutaneous transluminal coronary angioplasty
RBBB	Right bundle branch block
RCA	Right coronary artery
RCTs	Randomized controlled trials
RESTORE	Randomized Efficacy Study of Tirofiban for Outcomes and REstenosis trial
RLD	Refference lumen diameter
RV	Right ventricle
SD	Standard deviation
STEMI	ST segment elevation myocardial infarction
STR	ST segment resolution
TFGs	TIMI flow grades
TIGER-PA	Tirofiban Given in the Emergency Room before Primary Angioplasty
TIMI	Thrombolysis in myocardial infarction
TMPG	TIMI myocardial perfusion grade
t-PA	Tissue plasminogen activator
TVR	Target vessel revascularization
UA	Unstable angina
UFH	Unfractionated heparin
US	United states
uTVR	Urgent target vessel revascularization
VD	Vessel disease
VS	Versus
WHO	World health organization

INTRODUCTION

Primary percutaneous coronary intervention (PCI) is now the established reperfusion strategy in the treatment of acute myocardial infarction with ST-segment elevation (272). Nevertheless, myocardial damage is not immediately terminated after the elimination of epicardial occlusion with successful primary PCI. It has been presumed that reperfusion injury and embolization of epicardial thrombus and plaque debris jeopardize tissue-level perfusion (273).

Although thromboembolism of proximal origin may limit microvascular perfusion (274). A thrombus may also form in the microvasculature itself. This concept may help explain why randomized trials have failed to show a beneficial effect of distal protection devices on microvascular perfusion during primary PCI, despite effective retrieval of thrombus and plaque content from epicardial coronary arteries.(275)

The mechanisms underlying myocardial malperfusion after the restoration of epicardial blood flow are certainly likely to be multifactorial. The generation of oxygen free radicals, increased myocardial-cell calcium levels, cellular and interstitial edema, endothelial dysfunction, vasoconstriction, and thromboembolism have all been proposed (276). Injury to the endothelium also promotes a procoagulant milieu. Fibrin and platelet aggregates have been found in the coronary microvasculature of patients who have died of acute

myocardial infarction. In addition to fibrin formation, red-cell and platelet aggregation also contribute to microvascular occlusion and increased resistance in the microvasculature.

The extent of microvascular dysfunction has been shown to be an important and independent contributor to subsequent changes in left ventricular geometry and performance (277).

These benefits of PCI can further be enhanced by administration ofplatelet glycoprotein IIb/IIIa inhibitors abciximab(278), or eptifibatide (281).

Distal embolization of atherothrombotic material during primary percutaneous coronary intervention (PCI) is associated with impaired myocardial perfusion, abnormal left ventricular function, and higher mortality. At high local concentrations, glycoprotein IIb/IIIa receptor antagonists have been demonstrated to promote clot disaggregation in vitro (279).

Intracoronary administration of Eptifibatide in vivo may increase local drug concentration by several orders of magnitude and promote clot disaggregation with a minimal increase in systemic drug concentrations (279).

The intracoronary bolus alone application of eptifibatide during primary PCI may be safer and superior to the intravenous bolus (280).

Aim of the work

The aim of this work is to compare the effect of intracoronary bolus Versus intravenous bolus of eptifibatide followed by IV infusion as an adjunctive antiplatelet therapy on the efficacy and safety in patients with acute anterior ST segment elevation myocardial infarction undergoing primary percutaneous intervention.

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ACUTE MYOCARDIAL INFARCTION

Acute **myocardial infarction** (**AMI** or **MI**), commonly known as a **heart attack**, is a disease state that occurs when the blood supply to a part of the heart is interrupted. The resulting ischemia or oxygen shortage causes damage and potential death of heart tissue. It is a medical emergency, and the leading cause of death for both men and women all over the world.

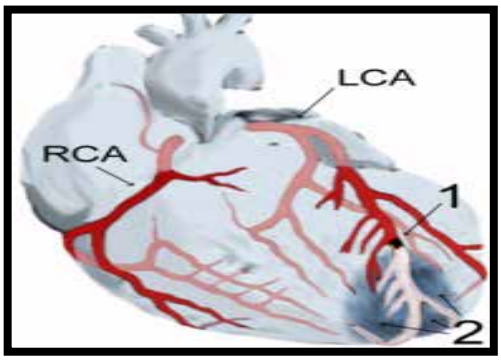

Figure (1): Diagram of a **myocardial infarction** of the tip of the anterior wall of the heart (an *apical infarct*) after occlusion (1) of a branch of the left coronary artery (LCA), right coronary artery = RCA **(1).**

· *Definition of myocardial infarction:*

Last updated definition of AMI is the "**Universal Definition of Myocardial Infarction**"**(2)** conducted by the Joint ESC/ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction:

Criteria for Acute Myocardial Infarction: The term myocardial infarction should be used when there is evidence of

myocardial necrosis (myocardial cell death) in a clinical setting consistent with myocardial ischaemia. Under these conditions any one of the following criteria meets the diagnosis for myocardial infarction:

1) Detection of rise and/or fall of cardiac biomarkers (preferably troponin) together with evidence of myocardial ischaemia with at least one of the following:
    - Symptoms of ischaemia;
    - ECG changes indicative of new ischaemia (new ST-T changes or new left bundle branch block [LBBB]);
    - Development of pathological Q waves in the ECG;
    - Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.

2) Pathological findings of an acute myocardial infarction

3) For percutaneous coronary interventions (PCI) in patients with normal baseline troponin values, elevations of cardiac biomarkers are indicative of peri-procedural myocardial necrosis. By convention, increases of biomarkers greater than 3 x 99th percentile URL have been designated as defining PCI-related myocardial infarction.
4) For coronary artery bypass grafting (CABG) in patients with normal baseline troponin values, elevations of cardiac biomarkers are indicative of peri-procedural myocardial necrosis. By convention, increases of

biomarkers greater than 5 x 99th percentile URL plus either new pathological Q waves or new LBBB, or angiographically documented new graft or native coronary artery occlusion, or imaging evidence of new loss of viable myocardium have been designated as defining CABG-related myocardial infarction.

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· *Clinical Classification of Different Types of Myocardial Infarction:*

Based on the universal definition of myocardial infarction: myocardial infarction was further classified into 5 different clinical types **(2):**

Type 1 (Spontaneous):

Spontaneous myocardial infarction related to ischaemia due to a primary coronary event such as plaque erosion and/or rupture, fissuring, or dissection

Type 2 (Secondary):

Myocardial infarction secondary to ischaemia due to either increased oxygen demand or decreased supply, e.g. coronary artery spasm, coronary embolism, anaemia, arrhythmias, hypertension, or hypotension

Type 3 (Sudden death):

Sudden unexpected cardiac death, including cardiac arrest, often with symptoms suggestive of myocardial ischaemia, accompanied by presumably new STelevation, or new LBBB, or evidence of fresh thrombus in a coronary artery by angiography and/or at autopsy, but death occurring before