Early versus very early invasive strategy after successful thrombolysis in patients with STEMI

Thesis for partial fulfillment of MD degree of cardiology

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LIST OF ABBREVIATIONS

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	Thrombosis 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

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Introduction

Acute myocardial infarction (AMI) remains a public health problem of epidemic proportions. Recent data from the American Heart Association (AHA) reveals a prevalence of myocardial infarction (MI) of 1.9-5.2%, which varies by age, sex, and ethnicity ***(American Heart Association, 2004).*** In the United States annually, there are 565,000 first-time, and 300,000 recurrent, myocardial infarctions ***(American Heart Association, 2004).*** Interestingly, in the last decade the National Registry of Myocardial Infarction (NRMI) have recorded a decrease in the percentage of patients with myocardial infarction who present with ST segment elevation (from 36% to 27%, $p \leq< 0.001$), while the percentage presenting without ST segment elevation has increased (from 45% to 63%, $p \leq<0.001$).

Primary percutaneous coronary intervention (PCI) in patients with acute myocardial infraction (AMI) has been shown to be preferable to thrombolytic therapy in terms of patient survival, higher rates of patency in the infarcted arteries, and lower rates of reinfarction and stroke ***(Weaver et al., 1998; Zijlstra et al., 1999).***

Till this time even with superiority of primary PCI most of patients with ST-elevation myocardial infarction present to

hospitals without percutaneous coronary intervention (PCI) facilities and receive fibrinolysis.

Early post thrombolysis referral had been discouraged in the past; however multiple studies were performed comparing immediate or early angiography after fibrinolysis versus a more conservative strategy of deferred PCI or ischaemia-guided management showed evidence for a reduction in the risk of total mortality in patients undergoing immediate or early PCI. There were no significant differences in the risk of stroke or major bleeding ***(D'Souza et al.,2010 and Borgia F et al.,2010).***

These results support the current recommendation for routine early invasive strategy in STEMI patients after successful fibrinolysis but the best timing for referral to invasive strategy still needs to be studied more in randomized trials.

Recent 2010 ESC revascularization guidelines stated that early routine invasive strategy post successful thrombolysis is class I level of evidence A, ***(William et al.,2010)*** however this strategy is not routinely applied in our country and best timing for intervention is needed to be studied.

Aim of the work

The aim of this work is to study the efficacy and safety of early versus very early coronary angioplasty for infarct related artery and hence best timing for invasive strategy post successful thrombolysis in patients presenting with STEMI.

Acute ST-segment Elevation Myocardial Infarction – Definition and Pathogenesis

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 ***(Luepker et al., 2003).***

Definition of Denovo Myocardial Infarction:

Recent "**Universal Definition of Myocardial Infarction**" put by the recent 2012 ESC guidelines ***(Thygesen K et al., 2012)*** as :-

Criteria for Acute Denovo Myocardial Infarction (without prior PCI or CABG): 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, it is defined as:

- Detection of rise and/or fall of cardiac biomarkers (preferably troponin) with at least one value above the 99th percentile of the upper reference limit (URL) together with evidence of myocardial ischemia with at least one of the following:

1- Symptoms of ischemia;

2- ECG changes indicative of new ischemia (new ST-T changes or new left bundle branch block [LBBB]);

3- Development of pathological Q waves in the ECG;

4- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality**.**

5- Identification of intracoronary thrombus by angiography or autopsy.

Risk Factors:

1- <u>Non-modifiable risk factors:</u>

- Older age
- Male gender ***(Wilson PM et al., 1998)***
- Family history of an early heart attack (before the age of 60), which is thought of as reflecting a genetic predisposition ***(Wilson PM et al., 1998)***

2- <u>Modifiable risk factors:</u>

- Cigarette smoking
- Dyslipidemia (especially high Low Density Lipoprotein and low High Density Lipoprotein)
- Diabetes (with or without insulin resistance)
- High blood pressure

- Obesity (defined by a body mass index of more than 30 Kg/m2, or alternatively by waist circumference (>120 cm in men and > 88 cm in women (Yusuf et al., 2005)
- Women using combined oral contraceptive pills ***(Khader et al., 2003)***

Some novel biochemical markers have been shown to be independent predictors of risk in ACS and in developing atherosclerosis especially in patients who experience life threatening ACS with few traditional risk factors ***(Brian et al., 2009)***. These biochemical markers fall into one of the following categories:

- Markers of necrosis: Troponin, CK-MB mass
- Markers of inflammation: High sensitivity C-reactive protein (hs-CRP), myeloperoxidase, pregnancy associated plasma proteins A, soluble CD-40 ligand, interleukin-6 and tumor necrosis factor (TNF).
- Markers of hemodynamic stress or neurohormonal activation: Brain natriuretic peptide (BNP) and N-terminal fragment of pro-brain natriuretic peptide (NT-pro BNP).
- Markers of coagulation: fibrinogen.
- Markers of vascular damage: Creatinin clearance and Cystatin C.
- Markers of accelerated atherosclerosis: hemoglobin A1c (HbA1c), proteogenomics. Others: lipoprotien a Lp(a) and homocysteine.