Primary PCI versus Early Routine Post Fibrinolysis PCI for ST Elevation Myocardial Infarction

Thesis Submitted for Partial Fulfillment of MD Degree in Cardiology

Submitted by

Ayman Mohamed Ahmed Fkirin Helal

M.B.B.CH, MSc Cardiology

Supervised By:

Doctor\ Sameh Mohamed Mamoun Shaheen

Professor of Cardiology
Faculty of Medicine – Ain Shams University

Doctor\ Walid Abdel-Azim Mohamed Elhammady

Professor of Cardiology
Faculty of Medicine – Ain Shams University

Doctor\ Mohamed Ismail Ahmed Ismail

Professor of Cardiology
Faculty of Medicine – Ain Shams University

Doctor\ Ahmed Samir Abdel-Hakim Ibrahim

Professor of Diagnostic Radiology
Faculty of Medicine – Ain Shams University

Doctor\ Lamyaa Elsayed Allam Elsayed

Lecturer of Cardiology
Faculty of Medicine – Ain Shams University

Faculty of Medicine
Ain Shams University
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Abstract

Background- Pharmaco-invasive strategy performed between 3 and 24 hours appears beneficial and safe. The rationale for following fibrinolysis with PCI is that many patients have a persistent reduction in flow in the infarct-related artery. The aim of the present study is to assess the effect of immediate fibrinolysis (with streptokinase "The widely available fibrinolytic in Egypt") in patients presented with acute STEMI followed by transferal and PCI within 3-24 hours compared to primary PCI and ischemia driven PCI on infarction size and microvascular obstruction.

Methods and Results- Sixty patients with first attack of acute STEMI within 12h were enrolled in this randomized multi-centers case-control study. The patients were randomized to 4 groups (15 patients each): primary PCI for patients presented to PPCI-capable centers (group I), transfer to PCI if presented to non-PCI capable center (group II), pharmaco-invasive strategy (group III) and fibrinolytic (streptokinase) and ischemia driven PCI (group IV). The primary endpoint is the infarct size assessed by cardiac MRI 3-5 days post MI. Death, reinfarction or disabling stroke were constitute the clinical (secondary) endpoints. The key safety (secondary) endpoint was be the incidence of major bleeding. The estimated patient delay was 6.1$\pm$2.5 hours with non-significant differences in the 4 groups. The system delay was 57$\pm$56, min in group I, 175.7$\pm$29 min in group II, 40.7$\pm$8.6 min in group III and IV. There was significantly larger infarction size in group IV compared to group I (49770$\pm$68449 vs. 28391$\pm$30322 mm^3, P=0.03), group II (49770$\pm$68449 vs. 28553$\pm$20006 mm^3, P=0.03) and group III (49770$\pm$68449 vs. 27580$\pm$20945 mm^3, P=0.02). But minor bleeding was significantly higher in group III compared to other groups due to puncture site related bleeding (33% of patients in group III vs. 13% in group IV vs. 0% in group I and II, P=0.006).

Conclusions- Compared to fibrinolysis followed by ischemia guided intervention, pharmaco-invasive strategy using streptokinase with PCI within 3-24 hours resulted in effective reperfusion and smaller infarction size in patients with acute STEMI. However, pharmaco-invasive strategy was associated with a slightly increased risk of minor bleeding.

Key words: pharmaco-invasive strategy, primary PCI, myocardial infarction, infarction size, cardiac MRI.

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4CH	Four chamber
ACC	American college of cardiology
ACS	Acute coronary syndrome
ADP	Adenosine di phosphate
AED	Automated external defibrillator
AHA	American heart association
ALS	Advanced life support
AMI	Acute myocardial infarction
aPTT	Activated partial thromboplastin time
ATM	Atmospheric pressure
AUC	Area under the curve
BI	Balloon inflation
BMI	Body mass index
BMS	Bare metal stent
BP	Blood pressure
BPM	Beat per minute
CABG	Coronary artery Bypass Graft
CAD	Coronary artery disease
CCU	Coronary care unit
CE	Contrast enhanced
CE-IR	Contrast enhanced - inversion recovery
CHD	Coronary heart disease
CHF	Congestive heart failure
CK	Creatinine kinase
CK-MB	Creatinine kinase – myocardial band
CMR	Cardiac magnetic resonance imaging
CPR	Cardiopulmonary resuscitation
D2B	Door to balloon
DAPT	Dual antiplatelet therapy
DBP	Diastolic blood pressure
DES	Drug eluting stent
DIDO	Door-in-door-out time
DM	Diabetes mellitus
ECG	Electrocardiogram

ED	Emergency department
EgSC	Egyptian society of cardiology
EMS	Emergency medical systems
EMS	Emergency medical service
ESC	European society of cardiology
EWS	Extended work space
FBS	Fasting blood sugar
FH	Family history
FMC	First medical contact
FOV	Field of view
FT	Fibrinolytic therapy
Gd	Gadolinium
GP	Glycoprotein
HDL	High density lipoprotein
HF	Heart failure
HR	Heart rate
HTN	Hypertension
IHD	Ischemic heart disease
IR	Inversion recovery
IRA	Infarct-related artery
JNC	Joint of national committee
JVP	Jugular venous pressure
LAD	Left anterior descending
LBBB	Left bundle branch block
LCX	Left circumflex
LDL	Low density lipoprotein
LGE	Late gadolinium enhancement
LM	Left main
LV	Left ventricle
LVEF	Left ventricular ejection fraction
MACCE	Major adverse cardiac and cerebrovascular event
MBG	Myocardial blush grade
MI	Myocardial infarction
MR	Mitral regurgitation
MRI	Magnetic resonance imaging
MVO	Micro vascular obstruction

NSTEMI	Non ST elevation myocardial infarction
PCI	Percutaneous coronary intervention
PET	Positron emission tomography
PPCI	Primary percutaneous coronary intervention
PTCA	Percutaneous transluminal coronary angioplasty
RCA	Right coronary artery
r-PA	Reteplase tissue plasminogen activator
RR	Respiratory rate
SA	Short axis
SBP	Systolic blood pressure
SFL	Stent for life
SK	Streptokinase
SPECT	Single photon emission computed tomography
SPSS	Statistical Package for Social Sciences
STEMI	ST elevation myocardial infarction
STR	ST-segment resolution
SWMA	Segmental wall motion abnormalities
TC	Total cholesterol
TFG	TIMI flow grade
TG	Triglyceride
TI	Inversion time
TIMI	Thrombolysis in myocardial infarction
TNK-tPA	Tenecteplase tissue plasminogen activator
tPA	Tissue plasminogen activator
UFH	Unfractionated heparin
URL	Upper range limit
VLA	Vertical long-axis
VSR	Ventricular septal rupture

Introduction

Worldwide, coronary artery disease (CAD) is the single most frequent cause of death. Over seven million people every year die from CAD, accounting for 12.8% of all deaths. Every sixth man and every seventh woman in Europe die from myocardial infarction. The in-hospital mortality of STEMI patients in the national registries of the European society of cardiology (ESC) countries varies between 6% and 14% ***(Steg et al, 2012)***.

Primary percutaneous coronary intervention (PCI) is an effective treatment for myocardial infarction with ST-segment elevation when it can be performed rapidly. However, primary PCI is performed in less than 25% of acute care hospitals in the United States ***(Cantor et al, 2009)***. Many patients with myocardial infarction with ST-segment elevation present to hospitals that do not have the capability of performing PCI and therefore cannot undergo PCI within the timelines recommended in the guidelines; instead, they receive fibrinolysis as the initial reperfusion therapy ***(Armstrong et al, 2013)***.

Despite the effectiveness and worldwide availability of intravenous thrombolysis, the usefulness of this therapy is greatly threatened by a high proportion of failed reperfusion and a substantial rate of reocclusion ***(Aviles et al, 2004)***.

Even if it is likely that fibrinolysis is successful, a strategy of routine early angiography is recommended if there are no contraindications. Several randomized trials and three contemporary meta-analyses have shown that early routine post-thrombolysis angiography with subsequent PCI (if required) reduced the rates of reinfarction and recurrent ischaemia compared with a 'watchful waiting' strategy, in which angiography and revascularization were indicated only in patients with spontaneous or induced severe ischaemia or LV dysfunction ***(Borgia et al, 2010).***

Thus, early referral for angiography with subsequent PCI (if indicated) should be the standard of care after thrombolysis: the so-called 'pharmaco-invasive' strategy. A crucial issue is the optimal delay between lysis and PCI. There was a wide variation in delay in trials, however a time window of 3–24 h after successful lysis is preferred ***(Stone, 2008)***.

Pharmaco-invasive strategy is now considered Class IIa level of evidence A in the recent ESC guidelines for STEMI ***(Steg et al, 2012)*** and level of evidence B in the recent ACC/AHA guidelines for STEMI ***(O'Gara et al, 2013).***

Several variants of tPA (tissue plasminogen activator) have been studied. Double-bolus r-PA (reteplase) does not offer any advantage over accelerated tPA, except for its ease of administration. Single-bolus weight-adjusted TNK-tPA (tenecteplase) is equivalent to accelerated tPA for 30-day mortality and is associated with a significantly lower rate of non-cerebral bleedings and less need for blood transfusion. Bolus fibrinolytic therapy is easier to use in the pre-hospital setting ***(Steg et al, 2012)***.

Aim of Work

The aim of the study is to assess the effect of fibrinolysis followed by PCI on infarction size and microvascular obstruction in patients presented with acute STEMI.