

Value of Thrombus Aspiration during Percutaneous Coronary Intervention in Acute ST- Elevation Myocardial Infarction

THESIS

*Submitted for Partial Fulfillment of MD Degree
In
Cardiovascular Medicine*

BY

Maged Ali Gubran Al-Basmi

SUPERVISORS

Prof. Hesham Salah Eldin Taha

*Professor of Cardiovascular Medicine
Faculty of Medicine - Cairo University*

Assist. Prof. Amr Hassan Mostafa

*Assist. Professor of Cardiovascular Medicine
Faculty of Medicine - Cairo University*

Dr. Reda Hussein Diab

*Lecturer of Cardiovascular Medicine
Faculty of Medicine - Cairo University*

Dr. Sameh Mohamed Elkaffas

*Lecturer of Cardiovascular Medicine
Faculty of Medicine - Cairo University*

*Faculty of Medicine
Cairo University*

2016

Abstract

Value of Thrombus Aspiration during Percutaneous Coronary Intervention in Acute ST- Elevation Myocardial Infarction

Background

Primary percutaneous coronary intervention (PPCI) reduces cardiac mortality in acute ST elevation myocardial infarction (STEMI) and is currently the preferred treatment. Several studies have shown that manual aspiration of the thrombus during PPCI can prevent distal embolization, improve myocardial reperfusion and improve clinical outcome.

The aim of our study was to determine the efficacy of thrombus extraction as adjunctive treatment before angioplasty for STEMI patients on mortality, recurrent myocardial infarction and the need for revascularization during hospitalization and the following 180 days, as well as to compare the different types of aspiration devices used during the study.

Subjects and methods

Two hundred and eleven patients were enrolled in the study with diagnosis of acute STEMI and planned for PPCI. PPCI with aspiration thrombectomy was done for 62 patients (aspiration group) and conventional PPCI (without aspiration thrombectomy) was done for 144 patients (control group). PPCI failed in five patients (2.3%). The aspiration group was subdivided into two subgroups according to the type of aspiration device used, Diver CE (32 patients) or Export (30 patients).

Results

There was no statistically significant difference between the aspiration and control groups regarding the mortality, myocardial infarction and need for revascularization (3.2%, 1.6%, and 6.5% compared to 3.5%, 1.4%, and 6.25 % respectively, p value > 0.05). There was no statistically significant difference between the Diver CE and Export groups regarding the mortality and myocardial infarction (0% and 3.1% compared to 6.7% and 0%, patients respectively, p value > 0.05), in contrary the difference in the need for revascularization was statistically significant favoring Diver CE (p value = 0.04).

Conclusion

We concluded that a strategy of manual aspiration thrombectomy in patients with STEMI who were undergone PCI, did not reduce the risk of all cause mortality, recurrent myocardial infarction, or the need for revascularization within 180 days, as compared with a strategy of PCI alone. There was no mortality benefit favoring Diver CE or Export aspiration devices. However, the need for revascularization was significantly lower with Diver CE aspiration device.

Keywords: STEMI, PPCI, aspiration thromboectomy, Diver CE, Export.



Acknowledgment

First and foremost, I feel always deeply indebted to "ALLAH", the Most Gracious and the Most Merciful.

*I would like to express my deepest gratitude and cardinal appreciation to **Prof. Hesham Salah Eldin Taha**, Professor of Cardiovascular Medicine, Faculty of Medicine, Cairo University, who kindly supervised and motivated the performance of this work, for his kind guidance and constant encouragement throughout this work as well as in my every day practice.*

*I am greatly honored to express my deep thankfulness to **Assist. Prof. Amr Hassan Mustafa** Assist. Professor of Cardiovascular Medicine, Faculty of Medicine, Cairo University, for his patience and meticulous supervision throughout the course of conducting this research. He is really so scientific, and so respectful.*

*I am greatly honored to express my sincere appreciation to **dr. Reda Hussein Diab**, lecturer of Cardiovascular Medicine, Faculty of Medicine, Cairo University, for his patience and meticulous supervision throughout the course of conducting this research. He is really so scientific, and so respectful.*

*I am greatly honored to express my deep thankfulness to **dr. Sameh Mohamed Elkaffas**, lecturer of Cardiovascular Medicine, Faculty of Medicine, Cairo University, for his patience and meticulous supervision throughout the course of conducting this research. He has enriched me with many ideas I earned much experience and technical tips from him.*

I am very grateful to all my staff members and my colleagues in the Department of Cardiovascular Medicine, Faculty of Medicine, Cairo University, for their help and support throughout the course of the work.

I am most grateful to my mother, my wife, my son and my daughters, my brothers and sisters for their patience and everlasting support. Finally, I want to dedicate this work to the memory of my father who encouraged me in my first steps of life.

Maged Ali Albasmi

CONTENTS

Chapter	Page
List of Abbreviations	I
List of Tables	IV
List of Figures	VI
Introduction and Aim of the Work	1
Review of Literature	3
ST- elevation myocardial infarction	3
Definition and diagnosis	3
Pathophysiology	10
Treatment	18
Thrombectomy	33
Aspiration thrombectomy	33
Mechanical thrombectomy	43
Assessment of myocardial perfusion and infarct size	48
Cardiac enzymes for infarct size assessment	50
Electrocardiographic assessment	52
Echocardiographic assessment	55
Angiographic assessment	64
Myocardial perfusion imaging.....	67
Magnetic resonance myocardial perfusion imaging.....	70
Subjects and methods	74
Results	83
Discussion	111
Limitations of the Study	120
Conclusions	121
Recommendations	122
Summary	123
References	125
Arabic Summary	

List of Abbreviations

ACC: American college of cardiology.

ACS: Acute Coronary Syndrome.

AHA: American Heart Association.

AMI: Acute Myocardial Infarction.

ASNC: American Society of Nuclear Cardiology.

BMS: Bare Metal Stent.

CAD: Coronary Artery Disease.

CABG: Coronary Artery Bypass Grafting.

CE MRI: Contrast Enhanced Magnetic Resonance Imaging.

CMR: Cardiac Magnetic Resonance.

CK: Creatine Kinase.

CKMB: Creatine Kinase Myocardial Band.

CT: Computer Tomography.

DAPT: Dual Antiplatelet Therapy.

DES: Drug Eluting Stent.

DS: Direct Stenting.

EACTS: European Association for Cardio-Thoracic Surgery.

ECG: Electrocardiography.

ED: Emergency Department.

EDV: End Diastolic Volume.

ESC: European Society of Cardiology.

ESV: End Systolic Volume.

FMC: First Medical Contact.

GFR: Glomerular Filtration Rate.

GP: Glycoprotein.

HF: Heart Failure.

ICH: Intracranial Hemorrhage.

IU: International Unit.

i.v.: Intravenous.

LBBB: Left Bundle Branch Block.

LV: Left Ventricle.

LVEF: Left Ventricular Ejection Fraction.

MACE: Major Adverse Cardiovascular Events.

MI: Myocardial Infarction.

MBG: Myocardial Blush Grade.

MRI: Magnetic Resonance Imaging.

NYHA: New York Heart Association.

PCI: Percutaneous Coronary Intervention.

PPCI: Primary Percutaneous Coronary Intervention.

RBBB: Right Bundle Branch Block.

RCT: Randomized Controlled Study.

RT: Rheolytic Thrombectomy.

STEMI: ST Elevation Myocardial Infarction.

STR: ST segment Resolution.

TA: Thrombus Aspiration.

TFG: TIMI Flow Grade.

TLR: Target Vessel Revascularization.

TIMI: Thrombolysis In Myocardial Infarction.

TNK: Tenecteplase.

UFH: Unfractionated Heparin.

USA: United States of America.

2D: Two Dimensional.

2DE: Two Dimensional Echocardiography.

3D: Three Dimensional.

List of Tables

Table	Title	Page
Table (1)	Comparison of cardiac markers for detection of myocardial necrosis	8
Table (2)	Routine therapies in the acute, subacute and long term phase of STEMI	32
Table (3)	Thrombus aspiration devices	38
Table (4)	Normal ranges and severity partition cutoff values for 2DE-derived LV EF	64
Table (5)	Definitions of TFG	65
Table (6)	Definitions of MBG	66
Table (7)	NYHA functional classification	75
Table (8)	The TIMI thrombus scale	81
Table (9)	Baseline clinical characteristics among the study groups	85
Table (10)	Laboratory investigations among the study groups	85
Table (11)	Cardiac enzymes among the study groups	86
Table (12)	ST segment resolution among the study groups	87
Table (13)	Location of MI among the study groups	87
Table (14)	EF value among the study groups	88
Table (15)	Drugs among the study groups	89
Table (16)	Duration of procedure among the study groups	89
Table (17)	Number of lesions among the study groups	90
Table (18)	Distribution of lesions among the study groups	91
Table (19)	Number of deployed stents among the study groups	92
Table (20)	Diameter and length of deployed stents among the study groups	92
Table (21)	Balloon dilatation among the study groups	93
Table (22)	Thrombus grading among the study groups	94
Table (23)	TIMI flow among the study groups	95
Table (24)	MBG among the study groups	96
Table (25)	Death, myocardial infarction and need for revascularization among the study groups	97

Table (26)	Baseline clinical characteristics among the study subgroups	99
Table (27)	Laboratory investigations among the study subgroups	100
Table (28)	Cardiac enzymes among the study subgroups	101
Table (29)	ST segment resolution among the study subgroups	101
Table (30)	Location of MI among the study subgroups	102
Table (31)	EF value among the study subgroups	102
Table (32)	Drugs among the study subgroups	103
Table (33)	Duration of procedure among the study subgroups	103
Table (34)	Number of lesions among the study subgroups	104
Table (35)	Distribution of lesions among the study subgroups	105
Table (36)	Number of deployed stents among the study subgroups	106
Table (37)	Diameter and length of deployed stents among the study subgroups	106
Table (38)	Balloon dilatation among the study subgroups	107
Table (39)	Thrombus grading among the study subgroups	107
Table (40)	TIMI flow among the study subgroups	108
Table (41)	MBG among the study subgroups	109
Table (42)	Death, myocardial infarction and need for revascularization among the study subgroups	110

List of Figures

Figure	Title	Page
Figure(1)	Reperfusion therapy for patients with STEMI	21
Figure(2)	Medtronic Export® Aspiration Catheter	37
Figure(3)	Sixteen-segment model for regional wall motion analysis	60
Figure(4)	Acute transmural infarct in a 60-year-old man with acute retrosternal pain and elevated cardiac enzyme levels	72
Figure (5)	Simpson's method for measurement of left ventricular ejection fraction, case	78
Figure(6)	Coronary artery map used by BARI investigators	80
Figure(7)	ST segment resolution among the study groups	87
Figure(8)	Ejection fraction measurement using Simpson's method. Apical 4 chamber views and apical 2 chamber views showed an EF of 40% measured during index presentation in a patient from Aspiration group with anterior STEMI.	88
Figure(9)	Distribution of lesions among the study groups	91
Figure(10)	Thrombus grading among the study groups	94
Figure(11)	Figure (A) shows left anterior oblique view with mid RCA occlusion and thrombus grade 5. Figure (B) shows left anterior oblique view) with distal LAD occlusion and thrombus grade 5.	94
Figure(12)	Figure (A) shows left anterior oblique view with mid RCA occlusion and TIMI flow 0 before intervention. Figure (B) shows the same view with TIMI flow III after intervention for the same case from the aspiration group.	95
Figure(13)	Figure (A) shows left anterior oblique view showing mid LAD occlusion with MBG grade 0 before intervention. Figure (B) shows MBG grade III after intervention for the same case from the aspiration group.	96
Figure(14)	Death, myocardial infarction and need for revascularization among the study groups	97
Figure(15)	Ejection fraction among the study subgroups	102
Figure(16)	Distribution of lesions among the study subgroups	105
Figure(17)	Thrombus grading among the study subgroups	108
Figure(18)	Figure (A) shows left anterior oblique view with proximal LAD occlusion and TIMI flow 0 before intervention. Figure (B) shows right anterior oblique view with TIMI flow III after intervention for the same case from Dive CE group.	109



Introduction and aim of work

ST-Elevation Myocardial Infarction (STEMI) is a clinical syndrome defined by characteristic symptoms of myocardial ischemia in association with persistent electrocardiographic (ECG) ST elevation and subsequent release of biomarkers of myocardial necrosis.¹

Acute myocardial infarction (AMI) is usually caused by rupture of a vulnerable plaque with a superimposed mural thrombus formation. This process, if not treated promptly, can lead to myocardial necrosis and heart failure. Percutaneous coronary intervention (PCI) is the treatment of choice for AMI.^{2,3} However, despite successful revascularization of the occluded epicardial coronary artery, PCI fails to achieve optimal TIMI-3 flow in 12% to 26% of cases, mainly because of the no-reflow phenomenon.⁴⁻⁶ No reflow can be defined as inadequate myocardial perfusion through a given segment of the coronary circulation without angiographic evidence of mechanical vessel obstruction.⁷ During PCI, mechanical debulking, through fragmentation, squeezing and pulverization, causes dislodgement and embolization of atherothrombotic debris composed of plaque and vessel wall constituents, including lipid, matrix, endothelial cells and platelet-rich thrombus. This process is thought to be responsible for the no-reflow phenomenon through microvascular obstruction caused by plugging by leukocytes, inflammation, edema and vasoconstriction.⁸ The purpose of pre-PCI thrombus aspiration, performed with extraction devices, is to reduce the intraluminal thrombus burden before balloon inflation and stent implantation, as well as reduce the risk of myocardial damage due to distal embolization of blood clot fragments and other microparticles in order to improve reperfusion.¹⁰



Several studies have compared PCI with and without pre-PCI thrombus aspiration to evaluate whether there is an added value in using extraction devices.^{6,9,11-19} Most of these studies found improved myocardial perfusion and reduced no-reflow incidence with thrombus aspiration. A meta-analysis published few years ago demonstrated that among patients with AMI treated with PCI, the use of adjunctive manual thrombectomy devices is associated with better epicardial and myocardial perfusion, less distal embolization, and significant reduction in 30 day mortality.²⁰

These studies were performed on non-selected patients with AMI. As expected, initial total coronary obstruction was present in many but not all patients, such as 55% in the TAPAS study⁶, 54.3% in the EXPIRA study¹⁷ and 64% in the REMEDIA study.¹¹

Few data are available in Egyptian patients, on the role of aspiration devices in patients presenting with acute STEMI. A study was needed to clarify the value of thrombus aspiration in this type of patients in a real life setting.

Aim of the work

- 1- To determine whether aspiration of thrombotic material before stent implantation of the infarct-related coronary artery results in improved myocardial perfusion and clinical outcome compared with conventional primary PCI in patients with STEMI.
- 2- To compare between different types of aspiration catheters used in those patients.



ST-Elevation Myocardial Infarction

Definition and Diagnosis

ST-Elevation Myocardial Infarction (STEMI) is a clinical syndrome defined by characteristic symptoms of myocardial ischemia in association with persistent electrocardiographic ST elevation and subsequent release of biomarkers of myocardial necrosis.¹ A working diagnosis of myocardial infarction must first be made. This is usually based on a history of chest pain lasting for 20 min or more, not responding to nitroglycerine. Important clues are a history of coronary artery disease (CAD) and radiation of the pain to the neck, lower jaw or left arm. The pain may not be severe. Some patients present with less-typical symptoms, such as nausea/vomiting, shortness of breath, fatigue, palpitations or syncope. These patients tend to present later, are more likely to be women, diabetic or elderly patients, and less frequently receive reperfusion therapy and other evidence-based therapies than patients with typical chest pain presentation. Registries show that up to 30% of patients with STEMI present with atypical symptoms.²¹ Awareness of these atypical presentations and a liberal access to acute angiography for early diagnosis might improve outcomes in this high-risk group.²²

The hallmark of the Third Universal Definition of MI³⁸⁶ is the detection of a rise and/or fall of cardiac biomarker values, with at least one of the values being elevated (i.e., > 99th percentile upper reference limit, URL).³⁸⁶ The preferred cardiac biomarker of necrosis is the highly sensitive and specific cardiac troponin (cTn). In addition, at least one of the five following diagnostic criteria should be met:

1. Symptoms of ischemia
2. New (or presumably new) significant ST/T wave changes or left bundle-branch block (LBBB)



3. Development of pathological Q waves on ECG
4. Imaging evidence of new loss of viable myocardium or regional wall motion abnormality
5. Identification of intracoronary thrombus by angiography or autopsy

Women often experience markedly different symptoms than men. The most common symptoms of MI in women include dyspnea, weakness, and fatigue. Fatigue, sleep disturbances and dyspnea have been reported as frequently occurring symptoms which may manifest as long as one month before the actual clinically manifested ischemic event. In women, chest pain may be less predictive of coronary ischemia than men.³⁸¹

Approximately one third of all myocardial infarctions are silent, without chest pain or other symptoms.³⁸² A silent course is more common in the elderly and in patients with diabetes mellitus.³⁸³

Diagnostic ST elevation in the absence of left ventricular (LV) hypertrophy or left bundle-branch block (LBBB) is defined by the European Society of Cardiology/ACC/AHA/World Heart Federation Task Force for the Universal Definition of Myocardial Infarction²³ as new ST elevation at the J point in at least 2 contiguous leads of ≥ 2 mm (0.2 mV) in men or ≥ 1.5 mm (0.15 mV) in women in leads V2–V3 and/or of ≥ 1 mm (0.1 mV) in other contiguous chest leads or the limb leads.²³

The majority of patients will evolve electrocardiographic evidence of Q-wave infarction. New or presumably new LBBB has been considered a STEMI equivalent. Most cases of LBBB at time of presentation, however, are “not known to be old” because of unavailability of a prior electrocardiogram for comparison. New or presumably new LBBB at presentation occurs infrequently, may interfere with ST-elevation analysis, and should not be considered diagnostic of acute myocardial infarction (MI) in isolation.²⁴ Baseline electrocardiographic abnormalities other than LBBB (e.g., paced rhythm, LV hypertrophy, Brugada



syndrome) may obscure interpretation. In addition, ST depression in ≥ 2 precordial leads (V1–V4) may indicate transmural posterior injury; multilead ST depression with coexistent ST elevation in lead aVR has been described in patients with left main or proximal left anterior descending artery occlusion.²⁵ Rarely, hyperacute T-wave changes may be observed in the very early phase of STEMI, before the development of ST elevation. Transthoracic echocardiography may provide evidence of focal wall motion abnormalities and facilitate triage in patients with ECG findings that are difficult to interpret. If doubt persists, immediate referral for invasive angiography may be necessary to guide therapy in the appropriate clinical context.^{26,27}

The electrocardiographic diagnosis may be more difficult in some cases, which nevertheless deserve prompt management. Among these are:

- Bundle branch block: in the presence of LBBB, the electrocardiographic diagnosis of acute myocardial infarction is difficult, but often possible if marked ST abnormalities are present. Somewhat complex algorithms have been offered to assist the diagnosis²⁸, but they do not provide diagnostic certainty.²⁹ The presence of concordant ST elevation (i.e. in leads with positive QRS deflections) appears to be one of the best indicators of ongoing myocardial infarction with an occluded infarct artery.³⁰ Previous data from thrombolysis trials have shown that reperfusion therapy is beneficial overall in patients with LBBB and suspected myocardial infarction. However, most LBBB patients evaluated in the emergency department do not have an acute coronary occlusion, nor do they require primary percutaneous coronary intervention (PPCI). A previous ECG may be helpful in determining whether the LBBB is new (and, therefore, the suspicion of ongoing myocardial infarction is high). Importantly, in