

**Epicardial Pad of Fat as a Predictive
of No-reflow following Primary PCI
for STEMI and its Correlation with
Mortality Risk using GRACE Score**

Thesis

*Submitted for Partial Fulfillment of Master Degree of
Cardiology*

By

Amr Salah Abdel Aal Mohamed

MBBch, Faculty of Medicine - Ain Shams University

Under Supervision of

Prof. Mona Abol Soud

Professor of Cardiology

Faculty of Medicine - Ain Shams University

Dr. Sameh Saleh Sabet

Assistant Professor of Cardiology

Faculty of Medicine - Ain Shams University

Dr. Maged Tewfik Saad Fahim

Lecturer of Cardiology

Faculty of Medicine - Ain Shams University

Faculty of Medicine - Ain Shams University

2016

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

Acknowledgment

*First and foremost, I feel always indebted to **ALLAH**, the Most Kind and Most Merciful.*

*I'd like to express my respectful thanks and profound gratitude to **Prof. Mona Abol Soud**, Professor of Cardiology- Faculty of Medicine- Ain Shams University for her keen guidance, kind supervision, valuable advice and continuous encouragement, which made possible the completion of this work.*

*I am also delighted to express my deepest gratitude and thanks to **Dr. Sameh Saleh Sabet**, Assistant Professor of Cardiology, Faculty of Medicine, Ain Shams University, for his kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.*

*I am deeply thankful to **Dr. Maged Tewfik Saad Fahim**, Lecturer of Cardiology, Faculty of Medicine, Ain Shams University, for his great help, active participation and guidance.*

I would like to express my hearty thanks to all my family for their support till this work was completed.

Last but not least my sincere thanks and appreciation to all patients participated in this study.

Amr Salah

List of Contents

Title	Page No.
List of Tables	i
List of Figures	ii
List of Abbreviations	iv
Introduction	1
Aim of the Work	3
Review of Literature	
▪ Coronary Microcirculation	4
▪ No-Reflow Phenomenon	9
▪ Epicardial Adipose Tissue	21
▪ ST Segment Elevation Myocardial Infarction	33
▪ Grace Score	74
Patients and Methods	79
Results	86
Discussion	94
Conclusion	105
Summary	107
References	109
Master Table	142
Arabic Summary	

List of Tables

Table No.	Title	Page No.
Table (1):	Nomenclature of body fat deposits	22
Table (2):	Comparison between group I and group II as regard age and gender.	87
Table (3):	Comparing both groups for prevalence of risk factors of CAD:.....	88
Table (4):	Represents the relevant clinical data between the two groups.	89
Table (5):	Comparing the 2 groups as regard vessel affection and TIMI flow.	91
Table (6):	Comparing the 2 groups as regard GRACE mortality risk	92

List of Figures

Fig. No.	Title	Page No.
Figure (1):	Schematic representation of the factors implicated in the interaction between endothelial and vascular smooth muscle cells during vasodilatation during physical stress	8
Figure (2):	Four interacting mechanisms that are responsible for no-reflow phenomenon.	13
Figure (3):	Diagnosis of no-reflow	17
Figure (4):	Visual appearance of microvascular obstruction (no-reflow) as black area at MCE and cardiac magnetic resonance as compared to what a normal study would look like	19
Figure (5):	Graphical representaion of the epicardial and paracardial fat and their relation to the pericarduim	22
Figure (6):	Epicardial fat measurement by echocardiography in the parasternal longitudinal axis	26
Figure (7):	Characterization of the pericardium, epicardial fat and paracardial fat by MRI end of diastole	28
Figure (8):	Characterization of the pericardium, epicardial fat and paracardial fat by CT scan	29
Figure (9):	Schematic diagram showing pathogenesis of myocardial infarct	39
Figure (10):	Site and referral of ischemic chest pain	43
Figure (11):	Normal for LBBB and paced rhythm	48
Figure (12):	STEMI in LBBB and paced rhythm	49
Figure (13):	Myocardial ischemia and subsequent myocardial injury can result from a variety of clinical entities	50
Figure (14):	Release of biomarkers into the circulation begins with prolonged ischemia and subsequent necrosis that results in loss of integrity of the cellular membranes	54
Figure (15):	System goals and initial reperfusion treatment of patients with STEMI	58

List of Figures (Cont...)

Fig. No.	Title	Page No.
Figure (16):	Delay times in relation to first medical contact.....	63
Figure (17):	Parasternal long axis view showing both Epicardial adipose tissue (EAT) and mediastinal adipose tissue (MAT).	82
Figure (18):	ROC curve for predicting significant GRACE.	86
Figure (19):	Comparing the prevalence of DM, hypertension (HTN), dyslipidemia (DL), smoking and peripheral vascular disease (PVD) in both groups.	89
Figure (20):	Comparing the 2 groups as regard more than one vessel affection and TIMI flow.	92
Figure (21):	GRACE mortality risk between both groups, on the right graph values are given as mean \pm 2SD, on the left graph values are given as median, range, and IQR (interquartile range) group II had GRACE mortality risk of mean 3.47 \pm 1.87, while group I had GRACE mortality risk of mean 2.05 \pm 1.	93
Figure (22):	Shows the correlation between the GRACE mortality risk and EAT thickness.	93
Figure (23):	Coronary angiography and ecocardiography for patient no (74)	94
Figure (24):	Coronary angiography and ecocardiography for patient no (5)	95

List of Abbreviations

Abb.	Full term
<i>ACEI</i>	<i>Angiotensin converting enzyme inhibitor</i>
<i>ACS</i>	<i>Acute coronary syndrome</i>
<i>AHA</i>	<i>American heart association</i>
<i>AMI</i>	<i>Acute myocardial infarction</i>
<i>BB</i>	<i>B receptor blocker</i>
<i>BMI</i>	<i>Body mass index</i>
<i>CABG</i>	<i>Coronary artery bypass graft</i>
<i>CAD</i>	<i>Coronary artery disease</i>
<i>CKD</i>	<i>Chronic kidney disease</i>
<i>DM</i>	<i>Diabetes mellitus</i>
<i>EAT</i>	<i>Epicardial adipose tissue</i>
<i>ESC</i>	<i>European society of cardiology</i>
<i>FH</i>	<i>Family history</i>
<i>GP IIb IIIa inhibitors</i>	<i>Glycoprotein IIb IIIa inhibitor</i>
<i>GRACE</i>	<i>Global Registry of Acute coronary events</i>
<i>HF</i>	<i>Heart failure</i>
<i>HR</i>	<i>Heart rate</i>
<i>HTN</i>	<i>Hypertension</i>
<i>IC</i>	<i>Intracoronary</i>
<i>IV</i>	<i>Intravenous</i>
<i>JVP</i>	<i>Jugular venous pressure</i>
<i>LV EF</i>	<i>Left ventricular ejection fraction</i>
<i>LV</i>	<i>Left ventricle</i>
<i>LVEDD</i>	<i>Left ventricular end diastolic diameter</i>
<i>LVESD</i>	<i>Left ventricular end systolic diameter</i>

List of Abbreviations (cont...)

Abb.	Full term
<i>MACE</i>	<i>Major adverse cardiac events</i>
<i>MBG</i>	<i>Myocardial blush grade</i>
<i>MR</i>	<i>Mitral regurgitation</i>
<i>MS</i>	<i>Metabolic syndrome</i>
<i>MVD</i>	<i>Multivessel disease</i>
<i>NSTACS</i>	<i>Non ST segment elevation acute coronary syndrome</i>
<i>PCI</i>	<i>Percutaneous coronary intervention</i>
<i>PVC</i>	<i>Pulmonary venous congestion</i>
<i>ROC</i>	<i>Recover operating characteristic curve</i>
<i>SBP</i>	<i>Systolic blood pressure</i>
<i>STEMI</i>	<i>ST segment elevation myocardial infarction</i>
<i>TIMI</i>	<i>Thrombolysis in Myocardial infarction</i>
<i>TTE</i>	<i>Transthoracic echocardiography</i>

ABSTRACT

This study was conducted on 113 patients who presented to the cardiology department of Ain Shams university hospital, with first acute anterior STEMI and underwent primary PCI. Patients admitted to the coronary care unit were analyzed thoroughly and data was recorded {Full history taking, clinical examination, 12 lead surface ECG, CK total and CK-MB, coronary angiographic details and transthoracic echocardiography in the first 48 hours}. Medical treatment of STEMI was given to subjects as per hospital protocol. All patients, during admission after AMI were subjected to echocardiographic evaluation of epicardial adipose tissue and LVEF. Patients were further divided into two groups using epicardial adipose tissue thickness of 5 mm as a cut off point, this number was derived from the ROC curve. **Group I:** Included patients EAT thickness less than 5 mms and it included 44 patients (38.9%). **Group II:** Included patients with EAT thickness greater than 5 mms and it included 69 patients (61.1%). Both groups were studied as regard epicardial adipose tissue thickness relation to the risk of no-reflow and to the mortality risk using GRACE score. Both groups were age and sex matched with homogenous risk factors for CAD. At univariate analysis for clinical data, group II (EAT > 5mm) showed statistically significantly increase in mortality risk using GRACE mortality risk, with no statistically significant difference as regard the location of infarction (anterior vs non anterior) BMI and pain to door time. Meanwhile for coronary angiographic data, univariate analysis showed statistically significant lower TIMI flow and statistically significantly greater multivessel affection in group II patients. The current study showed that epicardial fat thickness was significantly correlated with prognosis in patients with ACS. This suggests that echocardiographic epicardial fat thickness could be applied as predictive marker of prognosis in patients with ACS. EAT thickness determined on echocardiography may provide additional and substantial information on risk of no-reflow in STEMI patients treated with primary PCI.

Key words: Epicardial fat; no reflow.

INTRODUCTION

ST-elevation myocardial infarction is the most serious presentation of atherosclerotic coronary artery disease (ACAD) carrying the most hazardous consequences & patients with ST elevation are candidate for immediate reperfusion therapy ⁽¹⁾.

Primary percutaneous coronary intervention (PCI) is considered the preferred reperfusion modality for patients presenting with ST-segment elevation myocardial infarction (STEMI) ⁽¹⁾.

Severe Microvascular occlusion may manifest angiographically as reduced flow in the patent upstream epicardial arteries, a situation that is termed "no-reflow" or "slow flow" which is defined as less than TIMI III flow in absence of abrupt closure, high grade stenosis or flow limiting dissection and this event is associated with an increased infarct size, reduced recovery of ventricular function, further more this phenomenon is also linked to ventricular arrhythmia, early congestive heart failure or even cardiac rupture ⁽²⁾.

There are data on the relationship between epicardial adipose tissue thickness as a marker of microvascular disease and no-reflow ⁽³⁾.

Adipose tissue is known to affect the cardiovascular physiology via the release of active adipokines in paracrine

fashion (via local release and diffusion) or endocrine (via the systemic circulation) manner⁽⁴⁾.

Pericoronary EAT - released leptin prompts endothelial dysfunction, increased EAT thickness had been associated with coronary atherosclerosis progression and plaque vulnerability⁽⁵⁾.

Epicardial fat is true visceral fat located within proximity of the myocardium between the visceral pericardium and the myocardium, and it shares the same blood supply as the adjacent myocardium it also shows paracrine functions. This is the risky fat that is metabolically active⁽⁶⁾.

AIM OF THE WORK

To demonstrate the relationship between epicardial adipose tissue (EAT) thickness and no-reflow phenomena in patients undergoing primary PCI for acute STEMI as a marker of microvascular disease and its correlation with the risk of mortality using GRACE score.

Chapter 1

CORONARY MICROCIRCULATION

I- Anatomy of coronary microcirculation

Coronary vasculature can be divided into two anatomically & functionally different segments. The extramural coronary vasculature consists of large conduit coronary arteries & veins running on the epicardial surface of the heart, whereas the intramural coronary vasculature consists of smaller coronary arteries, arterioles and capillaries along with their accompanying vein within the myocardium itself⁽⁷⁾.

The intramural coronary circulation represents a complex vascular tree with a large number of branching orders and arborizations supplying the various vascular compartments of the myocardium. Ventricular branches with a perpendicular take off run vertically from the epicardium to the endocardium. Some of these branches reach the endocardium while others bifurcate at variable depths within the myocardium. In contrast, atrial branches ramify on the external surface without penetrating walls of the rather thin myocardium⁽⁸⁾.

An important components of the intramural system are the arterial-arterial anastomoses, also termed coronary artery collateral vessels. These vessels link intramural branches originating either from the same coronary artery or from different

coronary arteries. Also communications can be observed between intramural vessels and cardiac chambers⁽⁸⁾.

Small coronary arteries (150-400 μm) run intramyocardially and are, similarly to epicardial vessels, characterized by a monolayer of endothelial cells embedded with the tunica intima, internal elastic lamina, and several layers of tunica media, external elastic lamina and tunica adventitia⁽⁹⁾.

Coronary arterioles ($< 150 \mu\text{m}$) display a single layer of endothelial cells, two to three circular and concentric layers of smooth muscle cells and an outer adventitia⁽⁹⁾.

Myocardial capillaries (5-10 μm) are thin-walled structures containing a single layer of endothelial cells frequently associated with pericytes. Capillaries run parallel to myocardial fibers; usually two capillaries can be observed surrounding a single myocardial fiber. This symmetrical pattern is similar to the capillary networks observed in the striated muscles⁽⁹⁾.

II- Physiology of coronary microcirculation

Flow across the myocardium depends on the *pressure gradient* between the aortic root and the right atrium and the *resistance* of the coronary vasculature. Under normal conditions, the driving pressure is fully maintained along the epicardial conduit vessels with little if any pressure loss in the