INTRODUCTION

Acute myocardial infarction remains a leading cause of morbidity and mortality worldwide. It occurs when irreversible myocardial cell damage or death occur ***(Bolooki et al., 2010).***

ST segment elevation myocardial infarction is the most serious presentation of atherosclerotic coronary artery disease carrying the most hazardous consequences ***(Tosteson et al., 1996).***

ST segment elevation myocardial infarction is caused by occlusion of a major coronary artery and primary PCI is the preferred reperfusion strategy especially when performed by an experienced team within the shortest possible time from first medical contact ***(Werf et al., 2008)***.

Left ventricular remodeling is a relatively common and unfavorable event occurring after acute myocardial infarction. The extent of microvascular damage after reperfusion has been identified as one of the main determinant of this process ***(Galiutol et al., 2008; Carrabba et al., 2012)***

On the other hand, the opposite phenomenon; left ventricular volume reduction after coronary reperfusion; known as reverse left ventricular remodeling has been poorly investigated; especially after ST elevation myocardial infarction ***(Carrabba et al., 2012; Bellenger et al., 2005).***

Reverse remodeling is defined as a reduction more than 10% in left ventricular end systolic volume at 6 months follow up ***(Kwang et al., 2013; Gray Barn et al., 2008).***

Few data are available on the extent and prognostic value of reverse left ventricular remodeling after ST elevation myocardial infarction ***(Carrabba et al., 2012; Kwang et al., 2013).***

AIM OF THE WORK

To evaluate the incidence and predictors of left ventricular reverse remodeling 6 months after acute myocardial infarction in patients managed by primary PCI.

Chapter 1

ST SEGMENT ELEVATION MYOCARDIAL INFARCTION

Acute coronary syndrome (ACS) refers to acute myocardial ischemia caused by atherosclerotic coronary artery disease and includes ST-elevation myocardial infarction (STEMI), non ST-elevation MI (NSTEMI), and unstable angina (UA). These terms are used as a framework for guiding management. Patients with STEMI should be considered for immediate reperfusion therapy by thrombolytic agents or percutaneous coronary intervention (PCI) ***(Anderson et al., 2007).***

STEMI constitutes around 40% of acute myocardial infarction (AMI) and continues to be a major public health problem, both in developed as well as developing countries ***(Rogers et al., 2000)***.

Reperfusion therapy is the cornerstone of the treatment of patients with STEMI; it aims at reducing mortality and morbidity by achieving patency of the epicardial infarct-related artery (IRA) and by restoring myocardial tissue perfusion either pharmacologically or mechanically ***(Hellermann et al., 2002)***.

Definition and Diagnosis

STEMI is a clinical syndrome defined by characteristic symptoms of myocardial ischemia in association with persistent electrocardiographic (ECG) ST segment elevation and subsequent release of biomarkers of myocardial necrosis ***(Thygesen et al., 2012).***

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 Criteria of acute myocardial infarction ***(Thygesen 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 ischemia. 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:

- Symptoms of ischemia;
- ECG changes indicative of new ischemia (new ST segment –T wave 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.
- Identification of intracoronary thrombus by angiography or autopsy.

Universal Myocardial Infarction Classification *(Thygesen et al., 2012)*

Type 1: Spontaneous Myocardial Infarction

Spontaneous MI related to atherosclerotic plaque rupture, ulceration, fissuring, erosion, or dissection with resulting intraluminal thrombus in one or more of the coronary arteries that leads to decreased myocardial blood flow or distal platelet emboli with ensuing myocyte necrosis. The patient may have underlying severe CAD but on occasion non-obstructive or no CAD.

Type 2: Myocardial Infarction Secondary to Ischemic Imbalance

In instances of myocardial injury with necrosis in which a condition other than CAD contributes to an imbalance between myocardial oxygen supply and / or demand, e.g., coronary endothelial dysfunction, coronary artery spasm, coronary embolism, tachyarrhythmias / bradyarrhythmias, anemia, respiratory failure, hypotension, and hypertension with or without LV hypertrophy.

Type 3: Myocardial Infarction Resulting in Death When Biomarker Values Are Unavailable

Cardiac death with symptoms suggestive of myocardial ischemia and presumed new ischemic changes on the ECG or new LBBB but death occurring before blood samples could be obtained, before cardiac biomarkers could rise, or in rare cases, when cardiac biomarkers were not collected.

Type 4a: Myocardial Infarction Related to Percutaneous Coronary Intervention

MI associated with PCI is arbitrarily defined by elevation of cTn values to >5 × the 99th percentile of the URL in patients with normal baseline values ($\leq 99^{th}$ percentile of the URL) or a rise in cTn values >20% if the baseline values are elevated and are stable or falling. In addition, either (1) symptoms suggestive of myocardial ischemia, (2) new ischemic changes on the ECG

or new LBBB, (3) angiographic loss of patency of a major coronary artery or a side branch or persistent slow flow or no flow or embolization, or (4) imaging demonstration of new loss of viable myocardium or new regional wall motion abnormality is required.

Type 4b: Myocardial Infarction Related to Stent Thrombosis

MI associated with stent thrombosis is detected by coronary angiography or autopsy in the setting of myocardial ischemia and with a rise and/or fall in cardiac biomarkers values with at least one value above the 99th percentile of the URL.

Type 5: Myocardial Infarction Related to Coronary Artery Bypass Grafting

MI associated with CABG is arbitrarily defined by elevation of cardiac biomarker values to >10 × the 99th percentile of the URL in patients with normal baseline cTn values (<99th percentile of the URL). In addition, either (1) new pathologic Q waves or new LBBB, (2) angiographically documented new graft or new native coronary artery occlusion, or (3) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality is required.

Pathogenesis of STEMI:

The pathogenesis of coronary atherosclerosis is multi-factorial ***(Libby et al., 2001)***

Broadly, endothelial injury and dysfunction result in the adhesion and transmigration of leukocytes from the circulation into the arterial intima as well as the migration of smooth-muscle cells from the media into the intima, thus initiating the formation of an atheroma or atherosclerotic plaque ***(Libby et al., 2005).***

Atherosclerotic plaques cause progressive narrowing of the coronary arteries and eventually can cause a coronary occlusion. However, myocardial infarctions with ST-segment elevation are more typically caused by the sudden thrombotic occlusion of a coronary artery that previously was not severely narrowed. When such an occlusion occurs, the abrupt rupture, erosion, or fissuring of a previously minimally obstructive plaque creates a potent stimulus for platelet aggregation and thrombus formation ***(Freedman et al., 2005).***

Coronary Anatomy and Location of Infarction

Angiographic studies performed in the earliest hours of STEMI have revealed an approximately 90% incidence of total occlusion of the infarct-related vessel. Recanalization as a result of spontaneous thrombolysis diminishes angiographic

total occlusion in the period following the onset of MI. Pharmacologic fibrinolysis and PCI markedly increase the proportion of patients with a patent infarct-related artery early after STEMI.

A STEMI with transmural necrosis typically occurs distal to an acutely totally occluded coronary artery with thrombus superimposed on a ruptured plaque (see Fig. 1). Yet chronic total occlusion of a coronary artery does not always cause MI. Collateral blood flow and other factors such as the level of myocardial metabolism, the presence and location of stenosis in other coronary arteries, the rate of development of the obstruction, and the quantity of myocardium supplied by the obstructed vessel all influence the viability of myocardial cells distal to the occlusion. In many series of patients studied at necropsy or by coronary arteriography, a small number (5%) of those with STEMI had normal coronary vessels. An embolus that has lysed, a transiently occlusive platelet aggregate, or a prolonged episode of severe coronary spasm may have caused the infarct in these patients ***(Braunwald's Heart disease, Textbook of cardiovascular medicine, 10th edition, 2015)***

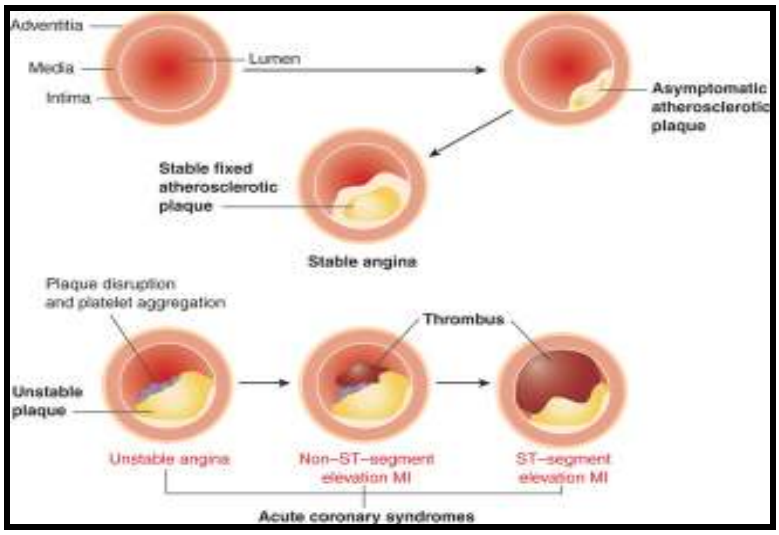

Figure (1): *Schematic diagram showing pathogenesis of myocardial infarct* ***(Carol et al., 2005)***

Characteristically, completely occlusive thrombi lead to transmural injury to the ventricular wall in the myocardial bed subtended by the affected coronary artery ***(figure 1)***. Infarction alters the sequence of depolarization ultimately reflected as changes in the QRS. The most characteristic change in the QRS that develops in most patients with STEMI is the evolution of Q waves in leads overlying the infarct zone ***(Wagner et al., 2009).***

In contrast, if blood flow is restored during the period of progressive necrosis, the ischemic myocardium is salvaged and the size of the infarct is reduced. Since morbidity and mortality from a myocardial infarction correlate with the size of the infarct, prompt restoration of blood flow would also be expected to improve left ventricular function and survival [Figure no.(3,4)] ***(Weir et al., 2006).***

Management of STEMI

Management including both diagnosis and treatment of AMI starts at the point of first medical contact (FMC), defined as the point at which the patient is either initially assessed by a paramedic or physician or other medical personnel in the pre-hospital setting, or the patient arrives at the hospital emergency department and therefore often in the outpatient setting ***(Tubaro et al., 2011).***

Diagnosis:

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.

Prodromal Symptoms

The patient's history remains crucial to establishing a diagnosis of STEMI. Chest discomfort resembling classic angina pectoris usually characterizes the prodrome, but it occurs at rest or with less activity than usual. Yet the symptoms are often not disturbing enough to induce patients to seek immediate medical attention, and if they do, they may not be hospitalized. A feeling of general malaise or frank exhaustion frequently accompanies other symptoms preceding STEMI.

CLINICAL PRESENTATION

Patient with UA/NSTEMI presented usually with chest pain which is severe in most of patients, and in some instances intolerable. The pain is prolonged, usually lasting for more than 30 minutes and frequently for a number of hours. It is usually constricting, crushing or compressing; and sometimes as a stabbing, knifelike, boring, or burning discomfort.

The pain is usually retrosternal in location, spreading frequently to both sides of the anterior chest, with predilection for the left side and usually radiates down the ulnar aspect of the left arm and the left wrist, hand, and fingers**.**

It may also radiate to the shoulders, upper extremities, neck, jaw, and interscapular region, again usually favoring the left side ***(Cannon et al., 2007).***

Women represent 30-45 percent of patients with unstable angina, 25 to 30 percent of patients with NSTEMI and approximately 20 percent of patients with STEMI.

In comparison to the STEMI, patients with unstable angina also have higher rates of prior MI, angina, previous coronary revascularization, and extra cardiac vascular disease ***(Hochman et al., 1999)***. Approximately 80 percent of patients with UA/NSTEMI have a history of cardiovascular disease and most have evidence of prior coronary risk factors ***(Khot et al., 2003)***.

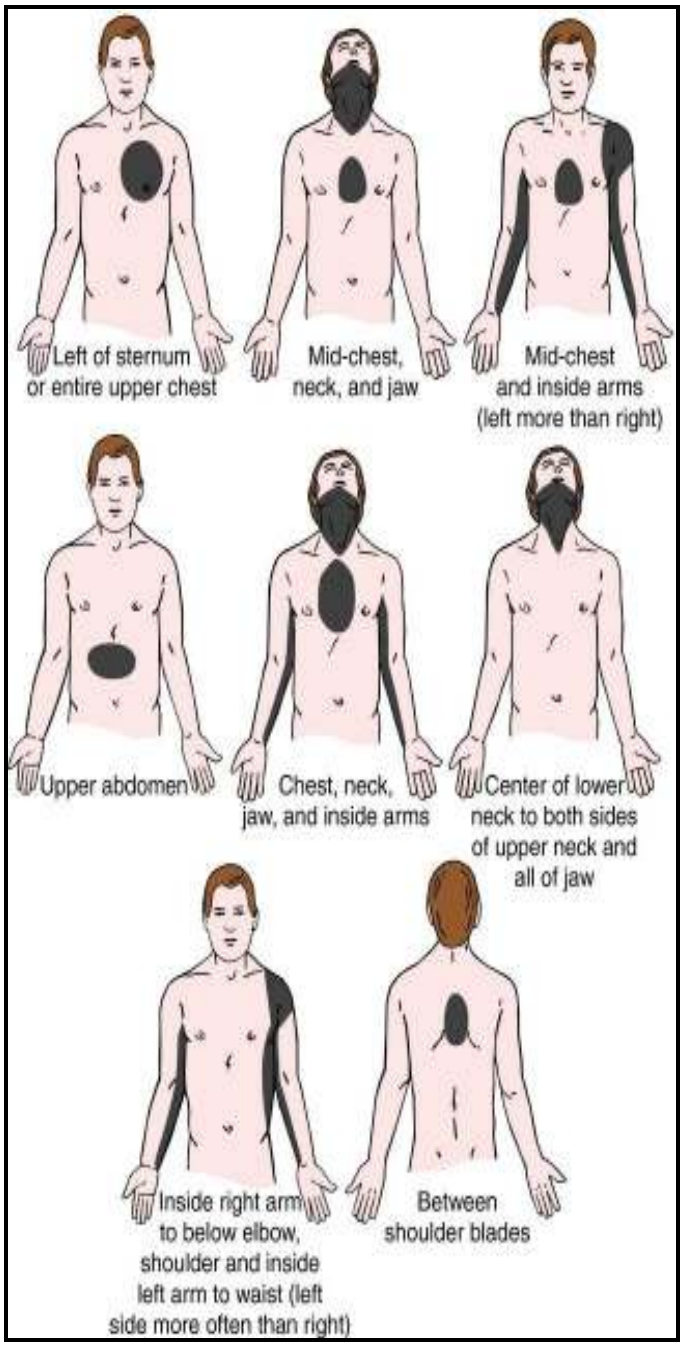

Figure (2): Site and referral of ischemic chest pain ***(Cannon et al., 2007)***

Silent ST-Elevation Myocardial Infarction with Atypical Features

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 a typical chest pain presentation. Registries show that up to 30% of patients with STEMI present with atypical symptoms ***(Brieger et al., 2009).***

Nonfatal STEMI can go unrecognized by the patient and be manifested only on subsequent routine electrocardiographic or postmortem examinations. Of these unrecognized infarctions, approximately half are truly silent, with patients unable to recall any symptoms whatsoever. The other half of patients with so-called silent infarction can recall an event characterized by symptoms compatible with acute infarction when leading questions are posed after the electrocardiographic abnormalities are discovered. Unrecognized or silent infarction occurs more commonly in patients without antecedent angina pectoris and in patients with diabetes and hypertension and are typically detected by identification of new wall motion abnormalities, fixed perfusion defects, or pathologic Q waves ***(Scirica, 2013).***