INTRODUCTION

Percutaneous coronary intervention (PCI) is accepted as the optimal strategy to re-canalize culprit coronary arteries in acute myocardial infarction [1]. Acute and long - term results of Primary PCI are optimized both by stents and by an aggressive medical anticoagulant regimen [2,3].

Percutaneous coronary intervention has traditionally been performed using femoral arterial access[4]. Risks associated with transfemoral approach (TFA) PCI include access site bleeding and major vascular complications, which are associated with a risk of subsequent morbidity, mortality, and costs[5].

Alternative vascular access sites for PCI include the brachial, radial, and ulnar arteries[6]. Data from multi-center and randomized trials comparing transradial approach (TRA) PCI with the TFA suggested a lower rate of bleeding and vascular complications associated with TRA PCI[7].

More recently, a large randomized trial of patients with acute coronary syndrome (ACS) undergoing coronary angiography or intervention, demonstrated that both radial and femoral approaches were equally effective and safe, with a lower rate of vascular complications in the radial approach[8].

In addition, the high-risk subgroup of patients with ST-segment elevation myocardial infarction (STEMI) associated

with more aggressive antithrombotic treatment than in elective or semi-urgent interventions had a reduction in cardiovascular events, driven by an apparent reduction in mortality in the TRA group[8]. However, lower bleeding risk with radial access may be counterbalanced by higher rates of procedural failure and longer procedural times, which may be detrimental in STEMI patients where timely reperfusion is critical.

The number of elderly patients undergoing percutaneous coronary intervention has increased over the last few decades. Studies have demonstrated that old age is a significant predictor of failure in procedures performed using the radial route and that it is associated with a greater need for conversion to an alternate access route[8,9].

In elderly patients, there is a greater incidence of tortuousness in the radial artery and in the brachiocephalic trunk[10]. However, old age is a significant risk factor for severe bleeding and vascular complications related to the procedure[11,12].

Although access through the radial artery is an attractive approach for PCI in elderly patients, due to its potential to reduce vascular complications and therefore to reduce bleeding, the technical challenges typically encountered using the radial approach and the potentially reduced rate of success of the procedure in these patients may discourage interventionists from using it in this scenario.

AIM OF THE WORK

The aim of the study is to evaluate safety (expressed as potential reduction of bleeding complications) in the TRA for primary PCI compared to TFA in over 55 years old patients presenting with STEMI who are referred for primary PCI, and to assess efficacy (expressed as door-to-balloon time) of TRA in comparison to TFA.

Chapter 1

ACUTE MYOCARDIAL INFARCTION

Background & Pathogenesis:

Acute myocardial infarction (MI) remains a leading cause of morbidity and mortality worldwide.[21,248] Myocardial infarction occurs when myocardial ischemia, a diminished blood supply to the heart, exceeds a critical threshold and overwhelms myocardial cellular repair mechanisms designed to maintain normal operating function and homeostasis. Ischemia at this critical threshold level for an extended period results in irreversible myocardial cell damage or death.[13]

Critical myocardial ischemia can occur as a result of increased myocardial metabolic demand, decreased delivery of oxygen and nutrients to the myocardium via the coronary circulation, or both. An interruption in the supply of myocardial oxygen and nutrients occurs when a thrombus is superimposed on an ulcerated or unstable atherosclerotic plaque and results in coronary occlusion.[13]

A high-grade (>75%) fixed coronary artery stenosis caused by atherosclerosis or a dynamic stenosis associated with coronary vasospasm can also limit the supply of oxygen and nutrients and precipitate an MI. Conditions associated with increased myocardial metabolic demand include extremes of physical exertion, severe hypertension (including forms of

hypertrophic obstructive cardiomyopathy), and severe aortic valve stenosis. Other cardiac valvular pathologies and low cardiac output states associated with a decreased mean aortic pressure, which is the prime component of coronary perfusion pressure, can also precipitate MI.[248]

Myocardial infarction can be subcategorized on the basis of anatomic, morphologic, and diagnostic clinical information. From an anatomic or morphologic standpoint, the two types of MI are transmural and non-transmural.[14]

A transmural MI is characterized by ischemic necrosis of the full thickness of the affected muscle segment(s), extending from the endocardium through the myocardium to the epicardium. A non-transmural MI is defined as an area of ischemic necrosis that does not extend through the full thickness of myocardial wall segment(s). In a non-transmural MI, the area of ischemic necrosis is limited to the endocardium or to the endocardium and myocardium. It is the endocardial and sub-endocardial zones of the myocardial wall segment that are the least perfused regions of the heart and the most vulnerable to conditions of ischemia.[14,255]

An older sub-classification of MI, based on clinical diagnostic criteria, is determined by the presence or absence of Q waves on an electrocardiogram (ECG). However, the presence or absence of Q waves does not distinguish a

transmural from a non-transmural MI as determined by pathology.[254]

A consensus statement was published to give a universal definition of the term myocardial infarction. The authors stated that MI should be used when there is evidence of myocardial injury (defined as an elevation of cardiac troponin values with at least one value above the 99th percentile upper reference limit) with a necrosis in a clinical setting consistent with MI.[18] Myocardial infarction was then classified by the clinical scenario into various subtypes.

Main types of acute MI should be considered: (Figure 1)

Type 1 MI: characterized by atherosclerotic plaque rupture, ulceration, fissuring, erosion, or dissection with resulting intraluminal thrombus in one or more coronary arteries leading to decreased myocardial blood flow and/or distal embolization and subsequent myocardial necrosis. The patient may have underlying severe coronary artery disease (CAD) but on occasion (i.e., 5% to 20% of cases), non-obstructive coronary atherosclerosis or no CAD, particularly in women. [15,16]

Type 2 MI: instances of myocardial necrosis in which a condition other than unstable coronary plaque contributes to an imbalance between myocardial oxygen supply and demand.

Mechanisms include coronary artery spasm, coronary embolism, coronary endothelial dysfunction, tachy/bradyarrhythmias, anemia, respiratory failure, hypotension, and severe hypertension. In addition, in critically ill patients and in patients undergoing major non-cardiac surgery myocardial necrosis may be related to injurious effects of pharmacologic agents and toxins. [18]

Type 3 MI is an MI resulting in sudden cardiac death. **Type 4a** is an MI associated with percutaneous coronary intervention, and **4b** is associated with in-stent thrombosis. **Type 5** is an MI associated with coronary artery bypass surgery.[18]

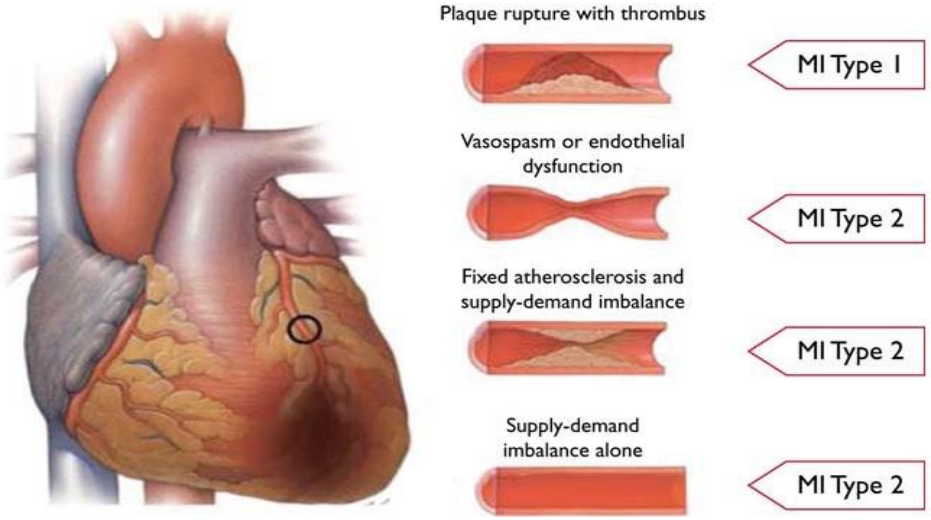

Figure (1): The differentiation between MI types 1 and 2 according to the condition of the coronary arteries. [15]

The leading symptom that initiates the diagnostic and therapeutic cascade is chest pain, but the classification of patients is based on the ECG.

Two categories of patients may be encountered: [19]

1. **Patients with acute chest pain and persistent (>20 min) ST-segment elevation:** This is termed ST-elevation ACS (STE-ACS) and generally reflects an acute total coronary occlusion. Most of these patients will ultimately develop an ST-elevation MI (STEMI). The therapeutic objective is to achieve rapid, complete, and sustained reperfusion by primary angioplasty or fibrinolytic therapy. (Figure 2)
2. **Patients with acute chest pain but without persistent ST-segment elevation:** These patients have rather persistent or transient ST segment depression or T-wave inversion, flat T waves, pseudo-normalization of T waves, or no ECG changes at presentation. The initial strategy in these patients is to alleviate ischemia and symptoms, to monitor the patient with serial ECGs, and to repeat measurements of markers of myocardial necrosis.

At presentation, the working diagnosis of non-ST-elevation ACS (NSTE-ACS), based on the measurement of troponins, will be further qualified as non-ST-elevation MI (NSTEMI) or unstable angina (UA). In a certain number of patients, coronary heart disease will subsequently be excluded as the cause of symptoms.

The distinction between STEMI and NSTEMI also does not distinguish a transmural from a non-transmural MI. The presence of Q waves or ST-segment elevation is associated with higher early mortality and morbidity; however, the

absence of these two findings does not confer better long-term mortality and morbidity.[20]

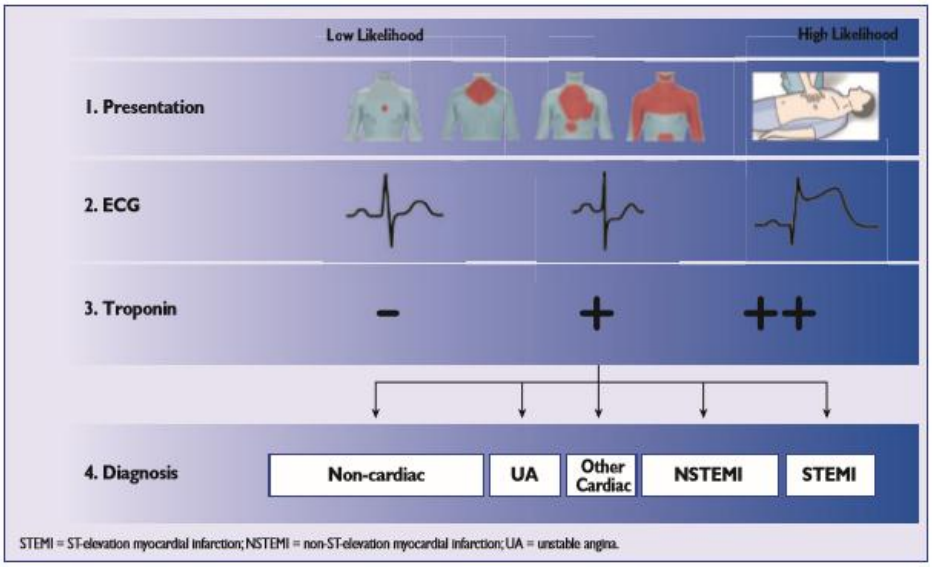

Figure (2): The spectrum of ACS.[19]

Prevalence and risk factors

Myocardial infarction is the leading cause of death in the United States and in most industrialized nations throughout the world. However, in Europe, there has been an overall trend for a reduction in ischaemic heart disease mortality over the past three decades.[21]

In Egypt approximately 107,000 people died from coronary disease in 2012 or 23.14% of total deaths, the age adjusted Death Rate is 186.36 per 100,000 of population ranks Egypt #23 in the world.[21]

The incidence of MI increases with age; however, the actual incidence is dependent on predisposing risk factors for atherosclerosis. Approximately 50% of all MIs in Egypt occur in people younger than 65 years.[21] However, in the future, as demographics shift and the mean age of the population increases, a larger percentage of patients presenting with MI will be older than 65 years.[21]

Six primary risk factors have been identified with the development of atherosclerotic coronary artery disease and MI: hyperlipidemia, diabetes mellitus, hypertension, tobacco use, male gender, and family history of atherosclerotic arterial disease. The presence of any risk factor is associated with doubling the relative risk of developing atherosclerotic coronary artery disease.

Signs and symptoms[26,256]

Acute MI can have unique manifestations in individual patients. The degree of symptoms ranges from none at all to sudden cardiac death. An asymptomatic MI is not necessarily less severe than a symptomatic event, but patients who experience asymptomatic MIs are more likely to be diabetic.

Despite the diversity of manifesting symptoms of MI, there are some characteristic symptoms.

- Chest pain described as a pressure sensation, fullness, or squeezing in the mid-portion of the thorax which may be

intermittent (usually lasting for several minutes) or persistent.

- Radiation of chest pain into the jaw or teeth, shoulder, arm, and/or back.
- Associated dyspnea or shortness of breath.
- Associated epigastric discomfort with or without nausea and vomiting.
- Associated diaphoresis or sweating.
- Syncope or near syncope without other cause.
- Impairment of cognitive function without other cause.

An MI can occur at any time of the day, but most appear to be clustered around the early hours of the morning or are associated with demanding physical activity, or both. Approximately 50% of patients have some warning symptoms (angina pectoris or an angina equivalent) before the infarct.

Initial diagnosis of STEMI:

Identifying a patient who is currently experiencing an MI can be straightforward, difficult, or somewhere in between. A straightforward diagnosis of MI can usually be made in patients who have a number of atherosclerotic risk factors along with the presence of symptoms consistent with a lack of blood flow to the heart. Patients who suspect that they are having an MI usually present to an emergency department. Once a patient's clinical picture raises a suspicion of MI, several confirmatory

tests can be performed rapidly. These tests include electrocardiography, blood testing, and echocardiography.

A working diagnosis of STEMI must first be made. This is usually based on symptoms consistent with myocardial ischaemia (i.e. persistent chest pain) and signs [i.e. 12-lead ECG]. Important clues are a history of CAD and radiation of pain to the neck, lower jaw, or left arm. Some patients present with less-typical symptoms such as shortness of breath, nausea/vomiting, fatigue, palpitations, or syncope. These patients tend to present later, are more likely to be women, diabetic or elderly patients.[22]

Registries show that up to 30% of patients with STEMI present with atypical symptoms. Awareness of these atypical presentations and a liberal access to acute angiography for early diagnosis might improve outcomes in this high-risk group.[23]

Timely diagnosis of STEMI is a key to a successful management. Latest ESC guidelines 2017 recommended that maximum time from FMC (First medical contact) to ECG and diagnosis should be less than 10 minutes.[26] ECG monitoring should be initiated as soon as possible in all patients with suspected STEMI to detect life-threatening arrhythmias and allow prompt defibrillation if indicated. A 12 lead ECG should be obtained and interpreted as soon as possible at the point of FMC.[23]

Electrocardiogram:

ECG criteria are based on changes of electrical currents of the heart (measured in millivolts). Standard calibration of the ECG is 10mm/mV. Therefore 0.1mV equals to 1mm square on the vertical axis. Typically, ST-segment elevation in acute myocardial infarction, measured at the J point, should be found in two contiguous leads and be ≥2.5 mm in men below the age of 40 years, ≥2 mm in men over the age of 40 years, or ≥1.5 mm in women in leads V2–V3 and/or ≥1 mm in other leads (in the absence of left ventricular (LV) hypertrophy or left bundle branch block (LBBB).[15,26] (Figure 3)

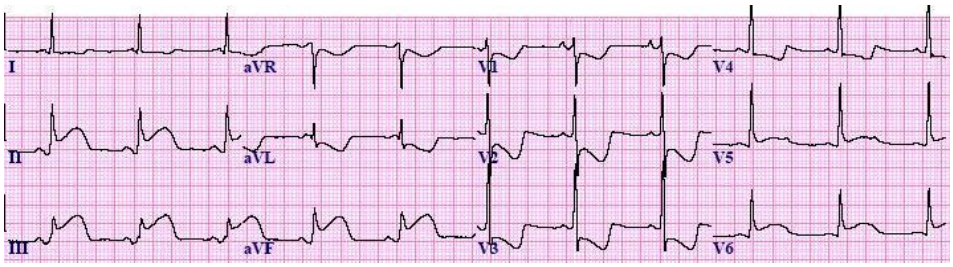

Figure (3): Inferior ST-segment elevation myocardial infarction.

In patients with inferior myocardial infarction, it is advisable to record right precordial leads (V3R and V4R) seeking ST elevation, in order to identify concomitant right ventricular infarction.[15,24] Likewise, ST-segment depression in leads V1–V3 suggests myocardial ischemia, especially when the terminal T-wave is positive (ST-elevation equivalent), and may be confirmed by concomitant ST elevation ≥0.5 mm recorded in leads V7–V9.[15,257]

The presence of ST-depression >1 mm in six or more surface leads, coupled with ST elevation in aVR and/or V1 but an otherwise unremarkable ECG, suggests ischemia due to multivessel or left main coronary artery obstruction, particularly if the patient presents with hemodynamic compromise.[25]

In the presence of LBBB, the ECG diagnosis of AMI is difficult but often possible if marked ST-segment abnormalities are present, patients with a clinical suspicion of ongoing myocardial ischaemia and LBBB should be managed in a way similar to STEMI patients, regardless of whether the LBBB is previously known. It is important to remark that the presence of a (presumed) new LBBB does not predict an MI per se.[26]

Blood sampling for serum markers:

Living myocardial cells contain enzymes and proteins (e.g., creatine kinase, troponin I and T, myoglobin) associated with specialized cellular functions. When a myocardial cell dies, cellular membranes lose integrity, and intracellular enzymes and proteins slowly leak into the blood stream[13]. These enzymes and proteins can be detected by a blood sample analysis. These values vary depending on the assay used in each laboratory. Given the acuity of a STEMI and the need for urgent intervention, the laboratory tests are usually not available at the time of diagnosis. Thus, good history taking and an ECG are used to initiate therapy in the appropriate