INCIDENCE OF DYSRHYTHMIAS IN ACUTE CORONARY SYNDROME

"EGYPTIAN REGISTRY"

Thesis

Submitted for Partial Fulfillment of Master Degree in Cardiology

By

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INTRODUCTION

Patients with ACS include those whose clinical presentations cover the following range of diagnoses: unstable angina, non – ST elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI). This ACS spectrum concept is a useful framework for developing therapeutic strategies ***(Zellweger et al., ٢٠٠٣).***

Cardiac arrhythmias are not uncommon during and immediately after an AMI. Of all patients who have an AMI, about ٩٠٪ develop some form of cardiac arrhythmia. In ٢٥٪ of patients, such rhythm abnormalities manifest within the first ٢٤ hours. In this group of patients, the risk of serious arrhythmias, such as ventricular fibrillation, is greatest in the first hour and declines thereafter. The incidence increases with an ST-elevation myocardial infarction (STEMI) and decreases with a non ST elevation myocardial infarction (NSTEMI) ***(Zellweger et al., ٢٠٠٣)***.

The clinician must be aware of these arrhythmias, in addition to reperfusion strategies, and he or she must treat those that require intervention to avoid exacerbation of ischemia and subsequent hemodynamic compromise. Most peri-infarct arrhythmias are benign and self limited. However, those that result in hypotension, increased myocardial oxygen requirements, and/or predisposes the patient to develop

additional malignant ventricular arrhythmias should be aggressively monitored and treated ***(Shah et al., ٢٠٠٥).***

Pathophysiology

AMI is characterized by generalized autonomic dysfunction that results in enhanced automaticity of the myocardium and conduction system. Electrolyte imbalances (e.g., hypokalemia and hypomagnesemia) and hypoxia further contribute to the development of cardiac arrhythmia ***(Zellweger et al., ٢٠٠٣).***

Contemporary evidence that in high risk post MI patients with LVEF < ٤٠٪ or frequent VPBs, the risk of AD was higher than that of NAD ***(Shah et al., ٢٠٠٥).***

In spite of significant reduction in total mortality observed in patients discharged after an acute myocardial infarction (MI), ventricular arrhythmias still account for ٣٠-٤٠٪ of deaths. This figure, which was initially provided by studies carried out in the pre-thrombolytic era, has been subsequently confirmed when most of the patients had been revascularized by thrombolysis or percutaneous coronary intervention (PCI) ***(Lombardi, ٢٠٠٥)***.

Early revascularization and more generalized use of beta blockers, angiotensin converting enzyme inhibitors, statins, and antiplatelet agents have largely contributed to the improvement in the prognosis of patients presenting with an ST elevation in acute MI. Nevertheless,

identification of patients at risk remains an issue far from being adequately addressed. There is a general consensus that depressed ventricular function, as reflected by a left ventricular ejection fraction (LVEF) < ٤٠٪, represents the strongest negative prognostic factor in these patients ***(Lombardi, ٢٠٠٥).***

AIM OF THE WORK

This study aims at the following:

- Showing the incidence of arrhythmias in acute coronary syndrome.
- Showing the Egyptian characteristics of acute coronary syndrome.

PATHOGENESIS OF ACUTE CORONARY SYNDROME (ACS)

Acute coronary syndromes (ACS), is a term which includes:

١. Unstable angina (UA),

٢. Non-ST-segment elevation myocardial infarction (NSTEMI)

٣. ST-segment elevation myocardial infarction (STEMI).

(Nikolsky and Stone, ٢٠٠٧)

Pathogenesis:

The allover mechanism of ACS results from demand perfusion imbalance ***(Coven et al., ٢٠٠٣)*** which is driven by various factors that include the following:

١. **Atherosclerosis mediated thrombus**

٢. **Coronary spasm**

٣. **Nonatherosclerotic**

They will be discussed as follows:

١. ***Atherosclerosis mediated thrombus:***

It is currently understood that atherogenesis is a complex interaction of risk factors including cells of the arterial wall, the blood and molecular messages that they exchange ***(Coven et al., ٢٠٠٣)***.

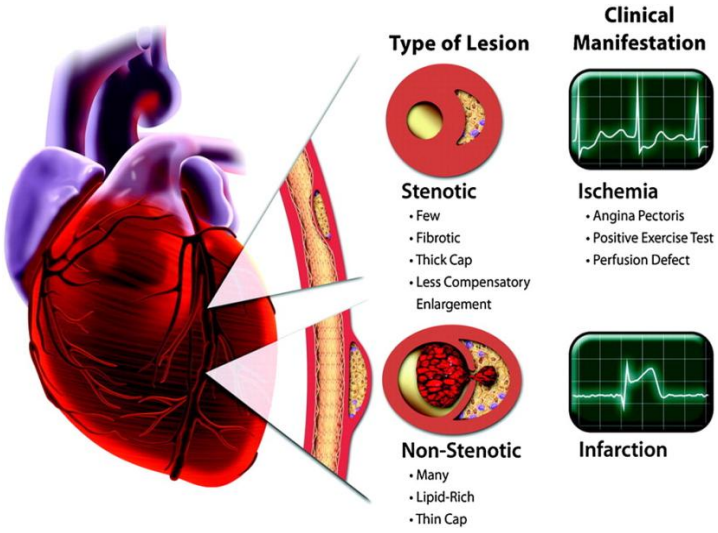

Figure (١): Atherosclerosis mediated thrombus ***(Yasue et al., ٢٠٠٧).***

An ACS develops when: a vulnerable or high-risk plaque undergoes disruption, which is a stimulus for thrombosis. Two types of thrombi can form, a platelet rich clot (referred to as a white clot) that forms in areas of high shear stress and only partially occludes the artery, or a fibrin-rich clot (referred to as a red clot) that is the result of an activated coagulation cascade and decreased flow in the artery. Red clots are frequently superimposed on white clots and this characteristic causes total occlusion. The severity of findings on coronary angiography frequently parallels the clinical severity of ACS. Mostly white clots are found in patients with non-ST elevation (NSTEMI) and red clots form in patients with ST segment elevation (STEMI) ***(Yasue et al., ٢٠٠٧)***.

١-١ The term of ACS is divided into:

a) Unstable angina and non-ST segment elevation myocardial infarction:

Results from rupture of an unstable arterial plaque leading to a "white" thrombus composed of platelets and fibrin, partial obstruction of the coronary artery, and subsequent reduced myocardial blood flow leading to ischemia and chest pain. These patients are at high risk for future events, such as myocardial infarction and death, and if not rapidly stabilized, they may develop coronary artery occlusion. In certain instances (< ٢٥٪ of cases), occlusion may occur in the presence of good collateral blood supply ***(Libby, ٢٠٠١)***.

b) ST segment elevation, or Q-wave, myocardial infarction:

Results from rupture of an unstable arterial plaque, leading to "red" thrombus formation, usually completely obstructing the vessel. The "red clot" is primarily composed of fibrin, but the formation of a white thrombus is a necessary step in the generation of the occlusive red clot therefore, patients with non-ST segment elevation ACS are at high risk for vessel occlusion, and therapy is targeted at prevention of this occlusion. Patients with occlusion are at high risk for extensive myocardial necrosis, The two types of non-ST segment elevation ACS and ST segment

elevation ACS are closely related in terms of pathophysiology but differ relative to ST segment elevation ACS with respect to the nature of the final thrombus, overall risk, and goals of management ***(Libby, ٢٠٠١)***.

١-٢ It is multifactorial: Consists of:

a) ***Endothelial injury*** results in the adhesion and transmigration of leukocytes from the circulation into the arterial intima

b) Migration of smooth muscle cells from the media into the intima.

c) Macrophages recruited into the artery wall become lipid laden foam cells by engulfing modified lipoproteins.

d) **Inflammatory mediators** cause the expression of procoagulant factor and matrix degrading proteinases that can weaken the fibrous cap of the plaque. If the fibrous cap ruptures coagulant factors in the blood can access the thrombogenic lipid core, causing thrombosis on a previously non occlusive atherosclerotic plaque. This process diminishes coronary artery perfusion through stenosis or by distal embolisation of the thrombus ***(Ramasamy Worcester Royal Hospital, ٢٠١١).***

٢. Coronary spasm

٢-١ *Characters of coronary spasm:*

a) It is unpredictable not induced by exercise, occurs particularly at rest from midnight to early morning

b) It is diagnosed by provocative tests and/or, by ambulatory ECG monitoring

٢-٢ *Risk factors:*

a) Age, it is a disease of middle aged men and postmenopausal women

b) Smoking

c) High sensitivity C reactive protein

٢-٣ *this can be explained by*

a) **NO** normally is responsible for the vascular tone in the basal state

b) **NO** is known to suppress the production of Endothelin and Angiotensin ٢, both of them are potent vasoconstrictors

c) Vasospasm is caused by either decreased production, or increased degradation of **NO**.

(Yasue et al., ٢٠٠٨)

٢-٤ *Mechanisms explaining this:*

a) <u>Polymorphisms of eNOS gene</u>

I. Endothelial NO is synthesized by endothelial NOS (e-NOS) which is constitutively expressed in the endothelium.

II. The e-NOS gene polymorphisms compromise the endothelial **NO** production and predispose the patients with these alleles to coronary spasm.

NO polymorphisms are found in only one-third of the patients and thus other genes or factors may also be involved in the pathogenesis of coronary spasm ***(Yasue et al., ٢٠٠٨)***.

b) <u>Oxidative stress:</u>

Oxygen free radicals degrade NO and cause vasoconstriction ***(Murad, ٢٠٠٦).***

Markers of oxygen species, are high in patients with coronary spastic angina***(Murad, ٢٠٠٦).***

Cigarette smoke extract markedly suppresses the ACh induced endothelium dependent relaxation. Smoking degrades NO by way of oxygen radicals ***(Moncada et al., ٢٠٠٦).***

Coronary spasm is more prevalent among smokers than in non-smokers ***(Moncada et al., ٢٠٠٦).***

٣. Nonatherosclerotic

٣-١ *Nonatherosclerotic causes of coronary stenosis can be found in:*

a) Patients with congenital anomalies of coronary arteries,

b) Collagen vascular disease

Valvular aortic stenosis or hypertrophic cardiomyopathy. ***(Ramasamy Worcester Royal Hospital, ٢٠١١)***

٣-٢ *Ischemia secondary to increased oxygen demand is found in:*

Fever, hyperthyroidism and sustained tachyarrythmias. Reduced coronary blood flow as in hypotension and, reduced myocardial oxygen delivery such as anemia or hypoxemia can precipitate unstable angina.

The chest pain syndrome of myocardial ischemia is similar regardless of whether the cause is intrinsic coronary atherosclerosis or other coronary and non coronary causes of myocardial ischemia ***(Ramasamy Worcester Royal Hospital, ٢٠١١)***