INTRODUCTION

Natriuretic peptides are released from the heart due to pressure and volume overload of the ventricle. During the last decade, B-type natriureticpeptide (BNP) has been proposed as a useful marker for the determination of acute and chronic left ventricular dysfunction and the severity of systolic left Ventricular dysfunction [1,2].

BNP is a 32-amino acid neurohormone synthesized in the form of pre-proBNP, which is firstly cleaved to pro-BNP, and then to active BNP and inactive fragment NTproBNP. In the first hours of acute myocardial infarction, BNP is released as a result of ischemia and necrosis of myocardial cells. Afterwards, BNP rises as a result of systolic and diastolic dysfunction and increased wall stress of the left ventricle [3,5].

There have been several evidences supporting that variation in plasma BNP level during acute phase of AMI can be used as a prognostic factor. New studies have shown that plasma BNP level, measured in acute coronary syndromes, independently might predict mortality rate, heart failure and degree of expansion of myocardial infarction [6, 7].

Although BNP plasma level is measured routinely in Acute myocardial infarction patients, but it is not full determined how is useful for estimation of left ventricular ejection fraction (LVEF), diastolic dysfunction and other acute complications [6, 7].

Aim of the Work

To investigate the prognostic value of B type natriuretic peptide (BNP) in acute myocardial infarction (AMI) patients and its correlation with left ventricular function and post-myocardial infarction complications in the in hospital period.

Chapter (1)

ACUTE ST SEGMENT ELEVATION MYOCARDIAL INFARCTION

Definition:

Acute ST elevation myocardial infarction is defined as retrosternal squeezing, aching, burning, or even sharp intense and unremitting chest pain for 30-60 minutes radiates up to the neck, shoulder, and jaw down to the ulnar aspect of the left arm and ECG criteria includes ST segment elevation in two or more contiguous leads greater than 2 mm (0.2 mV) for males and greater than 1.5 mm (0.15mV) in females if in leads V2 and V3 or greater than 1 mm (0.1 mV) if it is in other ECG leads or left bundle branch block (LBBB) that is believed to be new [(1)].

Risk factors:

Acute myocardial infarction is a multifactorial disease and there are thus several risk factors apart from age and gender. Most of these risk factors are life style related such as Type 2 diabetes and Insulin resistance, hypertension, general and abdominal obesity, dyslipidemia, metabolic syndrome, smoking, alcohol consumption [(2)].

Universal Classification of Myocardial Infarction:

Type 1: Spontaneous myocardial infarction:

This is an event related to atherosclerotic plaque rupture, ulceration, fissuring, erosion, or dissection with resulting intraluminal thrombus in one or more of the coronary arteries, leading to decreased myocardial blood flow or distal platelet emboli with ensuing myocyte necrosis. The patient may have underlying severe CAD but, on occasion (5 to20%), non-obstructive or no CAD may be found at angiography, particularly in women [(2-4)].

Myocardial infarction secondary to an ischemic imbalance (MI type 2):

In instances of myocardial injury with necrosis, where a condition other than CAD contributes to an imbalance between myocardial oxygen supply and/or demand, the term 'MI type 2' is employed (Figure 1). In critically ill patients, or in patients undergoing major (non-cardiac) surgery, elevated values of cardiac biomarkers may appear, due to the direct toxic effects of endogenous or exogenous high circulating catecholamine levels. Also coronary vasospasm and/or endothelial dysfunction have the potential to cause MI [(5-7)].

Cardiac death due to myocardial infarction (MI type 3):

Patients who suffer cardiac death, with symptoms suggestive of myocardial ischemia accompanied by presumed new ischemic ECG changes or new LBBB but without available biomarker values represent a challenging diagnostic group. These individuals may die before blood samples for biomarkers can be obtained, or before elevated cardiac biomarkers can be identified. If patients present with clinical features of myocardial ischemia, or with presumed new ischemic ECG changes, they should be classified as having had a fatal MI, even if cardiac biomarker evidence of MI is lacking[5-7].

Myocardial infarction associated with revascularization procedures (MI types 4 and 5):

Per procedural myocardial injury or infarction may occur at some stages in the instrumentation of the heart that is required during mechanical revascularization procedures, either by PCI or by coronary artery bypass grafting (CABG). Elevated cTn values may be detected following these procedures, since various insults may occur that can lead to myocardial injury with necrosis. It is likely that limitation of such injury is beneficial to the patient: however, a threshold for a worsening prognosis, related to an asymptomatic increase of cardiac biomarker values in the absence of procedural complications, is not well defined [12-14]. Subcategories of PCI-related MI are

connected to stent thrombosis and restenosis that may happen after the primary procedure [8–11].

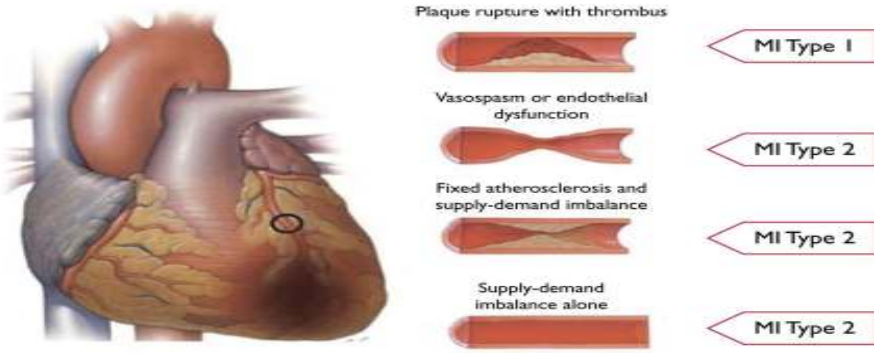

Figure (1): Universal Classification of Myocardial Infarction.

Pathological characteristics of myocardial ischemia and infarction:

MI is defined in pathology as myocardial cell death due to prolonged ischemia. After the onset of myocardial ischemia, histological cell death is not immediate, but takes a finite period of time to develop—as little as 20 min, or less in some animal models [15]. It takes several hours before myocardial necrosis can be identified by macroscopic or microscopic post-mortem examination. Complete necrosis of myocardial cells at risk requires at least 2-4 h, or longer, depending on the presence of collateral circulation to the ischemic zone, persistent or intermittent coronary arterial occlusion, the sensitivity of the myocytes to ischemia, pre-conditioning, and individual demand for oxygen and nutrients. The entire process leading to a healed

infarction usually takes at least 5-6 weeks. Reperfusion may alter the macroscopic and microscopic appearance [16].

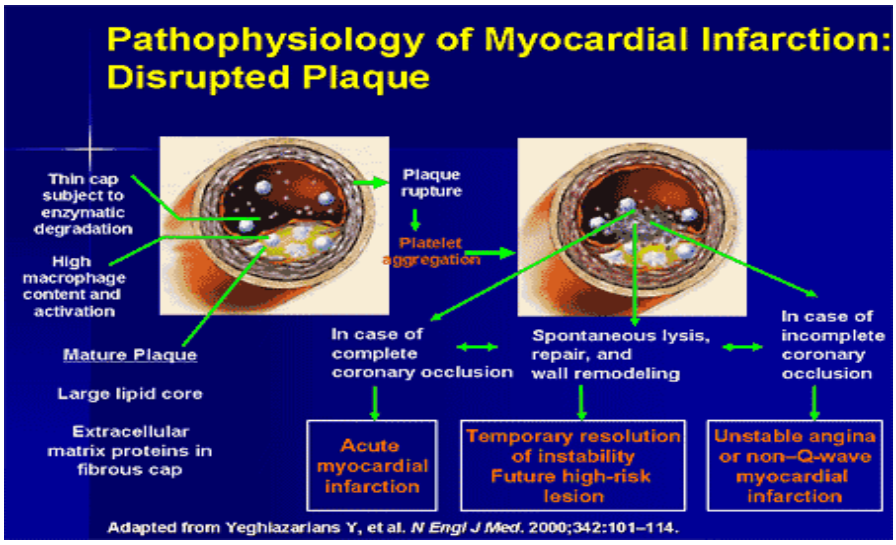

Figure (2): Pathophysiology of Myocardial infarction disrupted plaque

Complications following ST-segment elevation myocardial infarction

1. Hemodynamic disturbance

A- Heart failure:

Myocardial dysfunction frequently occurs during the acute and subacute phases following STEMI. Rapid improvement in ventricular function is usually seen following successful early revascularization of the infarct-related artery by PCI or thrombolysis. However, if the STEMI results in transmural injury and/or microvascular obstruction, especially of the anterior wall, pump failure with pathological remodeling

and the clinical symptoms and signs of heart failure may complicate the acute phase and result in chronic heart failure. Heart failure may also be the consequence of sustained arrhythmias or mechanical complications of STEMI [17].

The diagnosis of clinical heart failure during the acute and subacute phases of STEMI is based on typical symptoms such as dyspnoea, signs such as sinus tachycardia, a third heart sound or pulmonary rales, and some objective evidence of cardiac dysfunction, such as LV dilatation and reduced ejection fraction. Natriuretic peptides [B-type natriuretic peptide (BNP) and N-terminal pro-BNP] rise in response to increased myocardial wall stress and have been shown to be useful biomarkers in the management of patients with chronic heart failure [17].

LV dysfunction is the single strongest predictor of mortality following STEMI. The mechanisms responsible for LV dysfunction in the acute phase include myocardial loss and remodelling due to infarction, ischaemic dysfunction (stunning), atrial and ventricular arrhythmias and valvular dysfunction (pre-existing or new). There is frequently evidence of both systolic and diastolic dysfunction. Co-morbidities such as infection, pulmonary disease, renal dysfunction, diabetes or anaemia often contribute to the clinical picture. The degree of heart failure following myocardial infarction may be categorized according to the Killip classification: Class I, no rales or third heart sound; Class II, pulmonary congestion with

rales over,50% of the lung fields, sinus tachycardia or third heart sound; Class III, pulmonary oedema with rales over 50% of the lung fields and Class IV, cardiogenic shock [18].

1. Hypotension:

Is defined as persistent systolic blood pressure,90 mmHg. It may be due to heart failure but also to correctable hypovolaemia, treatable rhythm disturbance or mechanical complications. If prolonged, hypotension may cause renal dysfunction, acute tubular necrosis and reduced urinary output[18].

2. Pulmonary congestion:

Is characterized by dyspnoea with basal pulmonary rales, reduced arterial oxygen saturation, pulmonary congestion on chest X-ray and clinical response to diuretic and/ or vasodilator therapy [19].

3. Low output states:

Combine signs of poor peripheral perfusion and hypotension, renal dysfunction and reduced urinary output. Echocardiography may reveal poor left ventricular function, a mechanical complication or right ventricular infarction [18].

4. Cardiogenic shock:

Complicates 6–10% of all cases of STEMI and remains a leading cause of death, with hospital mortality rates approaching 50%. Although shock often develops early after the onset of acute myocardial infarction, it is typically not diagnosed on hospital presentation [(19)].

we should emergently revascularize Occluded coronaries for Cardiogenic shock (SHOCK) trial registry, of the patients who eventually developed shock during hospitalization, this occurred within 6 h in about 50% and within 24 h in 75% [(20)].

There is a wide spectrum of clinical symptoms, signs and haemodynamic findings that define the presence and severity of cardiogenic shock and are directly related to short-term outcome [(21-23)].

Patients typically present with hypotension, evidence of low cardiac output (resting tachycardia, altered mental status, oliguria, cool peripheries) and pulmonary congestion. The haemodynamic criteria for cardiogenic shock are a cardiac index of 2.2 L/min/m2 and an increased wedge pressure of 18 mmHg. Additionally, diuresis is usually 20 mL/h [(22)].

Shock is also considered present if i.v. inotropes and/or an IABP is needed to maintain a systolic blood pressure 90 mmHg. It is usually associated with extensive LV damage, but mayoccur in right ventricular infarction [(23)].

Both short- and long-term mortality appear to be associated with initial LV systolic dysfunction and the severity of mitral regurgitation [22]. The presence of right ventricular dysfunction on early echocardiography is also an important predictor of an adverse prognosis, especially in the case of combined left- and right ventricular dysfunction [23].

Baseline and follow-up stroke volume index and follow-up stroke work index appear to be the most powerful haemodynamic predictors of 30-day mortality in patients in cardiogenic shock and are more useful than traditional haemodynamic variables [24].

Therefore, cardiogenic shock characterization and management do not necessarily need invasive measurement of LV filling pressure and cardiac output through a pulmonary catheter but LV ejection fraction and associated mechanical complications should be evaluated urgently by two dimensional Doppler echocardiography [21-24].

B) Arrhythmias and conduction disturbances:

Arrhythmias and conduction disturbances are common during the early hours after myocardial infarction. According to recordings from cardiac monitors implanted within 11 +5 days of an acute myocardial infarction, the incidence is 28% for new-onset atrial fibrillation, 13% for non-sustained ventricular tachycardia, 10% for high-degree atrioventricular block (≤30

beats per minute lasting for ≥8 s), 7% for sinus bradycardia (≤30 beats per minute lasting for ≥8 s), 5% for sinus arrest (≥5 s), 3% for sustained ventricular tachycardia, and 3% for ventricular fibrillation [25]. The long term prognostic significance of early (,48 h) VF or sustained ventricular tachycardia (VT) in patients with acute myocardial infarction is still controversial. In patients with acute myocardial infarction, early VF/VT identified those at increased risk for 30-day mortality (22% vs. 5%) as compared to those without VF/ VT[26].

ACE inhibitors/ARBs reduced the 30-day mortality in these patients. Other studies have confirmed that beta-blocker therapy, given in the first 24 h after AMI in patients with early sustained VF/VT, was associated with decreased early mortality without worsening heart failure [27].

Prospective randomized studies are warranted to clarify the clinical implications of early-onset ventricular arrhythmias in this setting. Arrhythmias after the early reperfusion period may be a manifestation of a serious underlying condition, such as continuing myocardial ischaemia, pump failure, altered autonomic tone, hypoxia, and electrolyte- (e.g. hypokalaemia) and acid-base disturbances, all of which require attention and corrective measures [26-27].

High-degree atrioventricular block was a more powerful predictor of cardiac death than tachyarrhythmias in patients

with left ventricular ejection fraction,40% after myocardial infarction [25].

1. Supraventricular arrhythmias:

Atrial fibrillation complicates some 6–28% of myocardial infarctions and is frequently associated with severe LV damage and heart failure. Episodes may last from minutes to hours and are often repetitive. In many cases, the arrhythmia is well tolerated and no specific treatment is required, other than anticoagulation. In some instances, the fast ventricular rate contributes to heart failure, requiring prompt treatment [25-28].

Adequate rate control is important in order to reduce myocardial oxygen demand, and can be accomplished by administration of beta blockers or possibly calcium antagonists, either orally or intravenously. In patients with extensive myocardial damage or severe LV dysfunction, rate control is more safely achieved with i.v. digoxin with or without concomitant administration of i.v. amiodarone, related to the negative inotropic effect of beta-blockers or calcium antagonists. Urgent electrical cardioversion may be considered in patients presenting with atrial fibrillation and intractable ischaemia or haemodynamic instability [25-28].

Several, but not all, studies have suggested that development of atrial fibrillation in the setting of acute myocardial infarction is an independent predictor of all-cause

mortality, irrespective of the treatment given. Atrial fibrillation not only increased the risk for ischaemic stroke during the hospitalization but also during follow-up, even paroxysmal atrial fibrillation (AF) that has reversed to sinus rhythm at the time of discharge. Patients with atrial fibrillation and risk factors for thromboembolism should therefore be adequately treated with oral anticoagulation [25-29].

Other supraventricular tachycardias are rare and are usually self-limited. They may respond to vagal manoeuvres. Intravenous adenosine may be considered in this setting, if atrial flutter is ruled out and the haemodynamic status is stable; the ECG should be monitored during administration. If not contraindicated, beta blockers may be effective. Electrical cardioversion should be employed if the arrhythmia is poorly tolerated [25-29].

2. Ventricular arrhythmias:

Ventricular premature beats: are almost universal on the first day of the acute phase and complex arrhythmias (multiform complexes, short runs or the R-on-T phenomenon) are common. Their value as predictors of VF is questionable. No specific therapy is required.

***Ventricular tachycardia**:*

Should be differentiated from accelerated idioventricular rhythm a consequence of reperfusion that is usually harmless in which the ventricular rate is, 120 beats per minute. Runs of non-sustained VT (lasting, 30 s) are not reliable predictive markers for early VF and may be well tolerated, not necessarily requiring treatment [(30)].

More prolonged episodes may cause hypotension and heart failure and may degenerate into VF. Since there is no evidence that suppression of asymptomatic non-sustained VT prolongs life, there is no indication to treat non-sustained VT, unless it is associated with haemodynamic instability. Electrical cardioversion (which requires sedation in conscious patients) is indicated if any VT persists and always indicated if the patient is haemodynamically unstable [(30)].

It is the safest method for termination of sustained VT in acute STEMI. If the patient appears haemodynamically stable, i.v. amiodarone, sotalol or lidocaine (if the VT is thought to be related to ongoing myocardial ischaemia) may be initiated for its termination, but conversion rates are low. Amiodarone is the only anti-arrhythmic agent without severe pro-arrhythmic effects in patients with reduced LV function, and is therefore the drug of choice in patients with reduced left ventricular function [(30)].