INTRODUCTION

Coronary artery bypasses (CABG)

Coronary artery disease (CAD) is the most common disease in world and leading causes of mortality in the west countries. In this disease myocardial perfusion is decreased because of arteriosclerosis, and may cause angina or infarction. In addition to medication, coronary artery bypass grafts surgery (CABGs) has been accepted currently as a treatment ***(Parvizi et al., 2009).***

Population receiving coronary artery bypasses (CABG):

An American Heart Association position statement 1999, declared that CABG is indicated if medical management does not satisfactorily control angina in patient with CAD or if the patient has > 50% obstruction of the left main coronary artery or 3-vessel disease with moderate or severe left ventricular dysfunction regardless of symptoms. The procedures were described in some details to provide the background for understanding conditions that might lead to risk for adverse outcomes ***(Rodriguez et al., 2000).***

Coronary Artery Bypass Grafting (CABG)

It requires median sternotomy to expose the heart, after which the heart is stopped and the patient is placed on a cardiopulmonary bypass pump.

- *Effects of cardiopulmonary bypass:*

Systemic inflammatory response

Cardiopulmonary Bypass (CPB) has been associated with some degree of major organ dysfunction since the earliest days of cardiac surgery. In the absence of infection or ischaemia, the concept of the "post-pump syndrome" or "Systemic Inflammatory Response Syndrome (SIRS)" is used ***(Butler et al., 1993).***

The clinical consequences of the inflammatory response vary from increased duration of hospital stay, to neurocognitive disorders, stroke, acute Lung injury, multiple organ failure and death. The life threatening complication Adult Respiratory Distress Syndrome (ARDS), occurs in 0.5 - 1.7% of CPB patients and can be associated with multiple organ failure, which carries a mortality of 50 - 92 % ***(Asimakopoulos et al., 1999).***

The mechanism of the inflammatory response in CPB multifactorial. It combines operative trauma with contact activation of circulating blood components by the artificial surface of the bypass circuit, ischemia to major organs and endotoxin release from the gut ***(McBride et al., 2000).***

Systemic activation of complement, platelets & leukocytes in turn lead to secretion of inflammatory mediators, such as IL-1, IL-6, IL-8 and TNF and generation of complement factors C3a, C5a and C5b-C9 (the membrane attack complex) ***(Chennoweth et al., 1999).***

These are thought to lead to systemic vascular endothelial activation and leukocyte sequestration in organs ***(Dreyer et al., 2000).***

Effect on glucose metabolism

Hyperglycemia usually accompanies the stress response associated with CPB. Hyperglycemia and impaired glucose control have been associated with worsened outcomes after myocardial infarction and acute coronary syndromes leads to stroke, postoperative wound infections, and severe head injury ***(Hylek et al., 2001).***

Insulin protocols and use of a glucose-insulin-potassium solution to ensure tight glucose control after cardiac surgery in adults have been associated with lower mortality, improved hemodynamics, .and decreased need for reoperations, as well as less renal failure Glucose monitoring during CPB and rapid correction of hypoglycemia with dextrose is essential for decreasing morbidity resulting from heart surgery ***(Furnary et al., 2003).***

Atrial fibrillation after bypass surgery:

With an incidence rate of 30-50%, atrial fibrillation (AF) after bypass surgery continues to be one of the most common complications, increases post-operative morbidity and resource utilization ***(Cresswell et al., 1999).***

There are major complications associated with coronary artery bypass graft surgery as death, myocardial infarction, stroke, wound infection, prolonged requirement for mechanical ventilation, acute kidney injury, and bleeding requiring reoperation ***(Fortescue et al., 2001).***

Respiratory function is still impaired when the patient is transferred to the postoperative floor, with many patients exhibiting shortness of breath with some splinting from chest wall discomfort. Arterial desaturation is not uncommon, and all patients should have an arterial saturation measured daily by pulse oximetry until the SaO2 remains above 90%. Most patients have some degree of fluid overload and require diuresis, and steps must be taken to overcome a poor inspiratory effort and atelectasis. Potential complications, such as pneumonia, bronchospasm, pleural effusions, or pneumothorax, can be identified by examination and a chest x-ray ***(Ng et al., 2002).***

Patients with some element of preoperative renal dysfunction, severe hypertension, postoperative low cardiac output syndromes, or those requiring substantial doses of

vasopressors may show evidence of gradual, progressive renal dysfunction. Diuretics are useful in reducing the immediate postoperative fluid overload and preventing the development of oliguric renal failure.

Heparin-induced thrombocytopenia (HIT) is a very serious complication of heparin therapy that may result in profound thrombocytopenia and widespread arterial and venous thrombosis. It carries a 20–30% mortality ***(Shorten and Comunale, 1996).***

Nosocomial infections develop in 10–20% of patients undergoing cardiac surgery. Such infections may produce bacteremia, but most commonly affect the surgical sites as well as the respiratory and urinary tracts. They commonly increase the length of stay and, because of their association with multisystem organ failure, they increase operative mortality by 4–5 fold ***(Spelman et al., 2000).***

Neurologic complications are dreaded sequelae of cardiac surgical procedures. Type 1 (focal) neurologic events complicate approximately 3% of coronary bypass operations performed on-pump with an additional 3% suffering type 2 (neurocognitive) deficits. The risk of cerebral embolization is greater in patients undergoing valve surgery and may be expected to increase as older patients with more advanced atherosclerosis undergo more complex surgical procedures ***(Lund et al., 2003).***

Gastrointestinal complications develop in 1–2% of patients undergoing open-heart surgery. The common pathophysiologic mechanism is a low cardiac output state, which produces sympathetic vasoconstriction, hypoperfusion, and hypoxia of the splanchnic bed. Inadequate tissue perfusion contributes to mucosal ischemia and the so-called acute GI focal necrosis syndrome. Changes that are seen may include stress ulceration, mucosal atrophy, bacterial overgrowth from stress ulcer prophylaxis, and loss of barrier function with increased permeability. These changes may potentially lead to bacterial translocation, sepsis, and multiorgan failure. Use of preventive measures and prompt, aggressive surgical intervention are necessary to decrease the mortality associated with these complications ***(Sanisoglu et al., 2004).***

AIM OF THE WORK

To evaluate the non cardiac complication after coronary artery bypass surgery.

Chapter 1

RISK FACTORS FOR CORONARY ARTERY DISEASE

- **Nontraditional or Novel Risk Factors**
- **Traditional Risk Factors**

Risk factors for coronary artery disease (CAD) were not formally established until the initial findings of the Framingham Heart Study in the early 1960s. The understanding of such factors is critical for a clinician to prevent cardiovascular morbidities and mortality. See the image below for traditional and nontraditional risk factor biomarkers ***(Howard et al., 2002).***

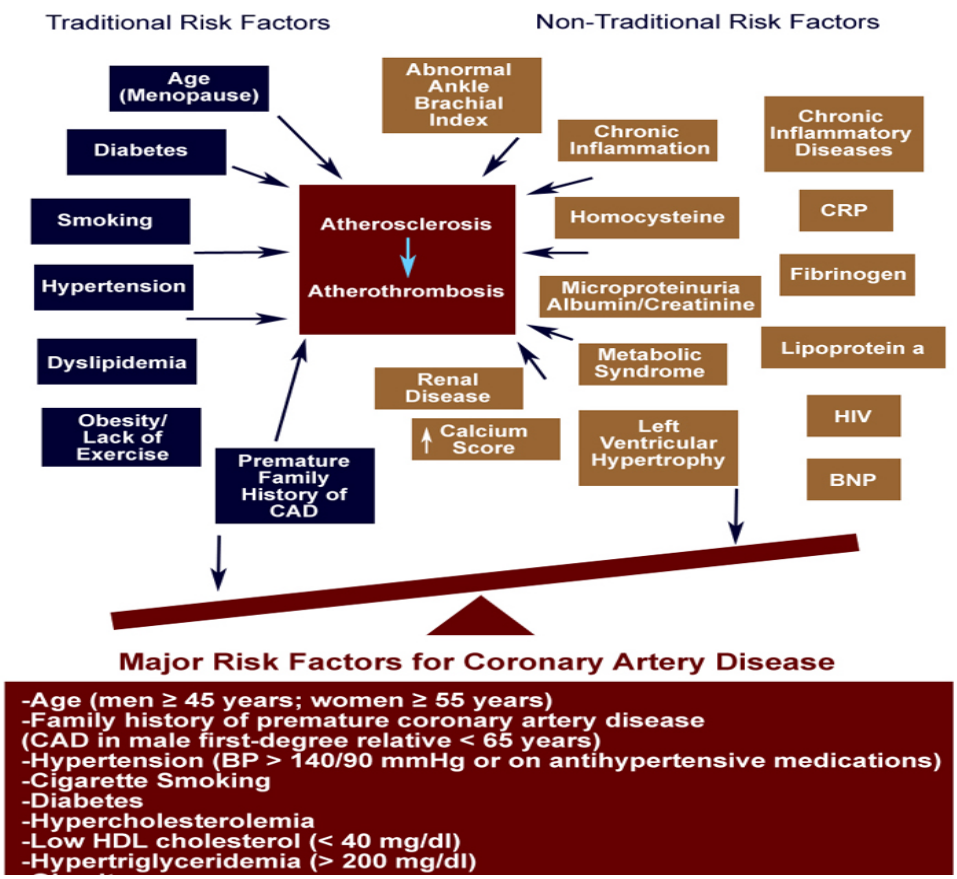

Fig. (1): Major risk factors for coronary artery disease

Traditional versus nontraditional risk factors for coronary artery disease (CAD). The expanding list of nontraditional biomarkers is outweighed by the standard risk factors for predicting future cardiovascular events and adds only moderately to standard risk factors. BNP = B-type natriuretic peptide; BP = blood pressure; CRP = C-reactive protein; HDL = high-density lipoprotein cholesterol; HIV = human immunodeficiency virus infection.

- *Nontraditional or Novel Risk Factors*

1- C-reactive protein

C-reactive protein (CRP) is a protein in the blood that demonstrates the presence of inflammation, which is the body's response to injury or infection; CRP levels rise if inflammation is present. The inflammation process appears to contribute to the growth of arterial plaque, and in fact, inflammation characterizes all phases of atherothrombosis and is actively involved in plaque formation and rupture ***(Rexrode et al., 1998).***

According to some research results, high blood levels of CRP may be associated with an increased risk of developing coronary artery disease (CAD) and having a heart attack In the Jupiter trial, in healthy persons without hyperlipidemia but with elevated high-sensitivity CRP levels, the statin drug rosuvastatin significantly reduced the incidence of major cardiovascular events ***(He M et al., 2010).***

The 2010 ACCF/AHA guideline for assessment of cardiovascular risk in asymptomatic adults states that measurement of C-reactive protein can be useful in selecting patients for statin therapy and may be reasonable for cardiovascular risk assessment, depending on the patient’s age and risk level. C-reactive protein measurement is not recommended for cardiovascular risk assessment in asymptomatic high-risk adults, low-risk men 50 years or younger, or low-risk women 60 years or younger ***(Micha et al., 2010).***

2- Lipoprotein (a)

An elevated lipoprotein (a) [LP (a)] level is an independent risk factor of premature CAD and is particularly a significant risk factor for premature atherothrombosis and cardiovascular events. Measurement of LP (a) is more useful for young individuals with a personal or family history of premature vascular disease and repeat coronary interventions. The 2010 ACCF/AHA guideline for assessment of cardiovascular risk in asymptomatic adults states that, in asymptomatic intermediate-risk adults, lipoprotein-associated phospholipase A2 might be reasonable for cardiovascular risk assessment ***(Micha et al., 2010).***

Lp(a) may be used to identify people at increased cardiovascular risk, but as of yet, there have been no studies on Lp (a) lowering because of the lack of available agents that are effective in reducing this value. Therefore, low-density lipoprotein (LDL) lowering is probably the best strategy in people with elevated LP (a) levels ***(Thompson et al., 2003).***

3- Homocysteine

Homocysteine is a natural product of the dietary breakdown of protein methionine. In the general population, mild to moderate elevations are due to insufficient dietary intake of folic acid. Homocysteine levels may identify people at increased risk of heart disease, but again, due to the lack of agents that effectively alter the homocysteine levels ***(Paynter et al., 2011).***

4- Tissue plasminogen activator

An imbalance of the clot dissolving enzymes (eg, tissue plasminogen activator [tPA]) and their respective inhibitors (plasminogen activator inhibitor-1 [PAI-1]) may predispose individuals to myocardial infarctions ***(Nordmann et al., 2011).***

5- Small, Dense LDL

Individuals with a predominance of small, dense LDL particles are at increased risk for CAD. Thus, core lipid composition and lipoprotein particle size and concentration may provide a better measure of cardiovascular risk prediction ***(Manson et al., 2003).***

6- Fibrinogen

Levels of fibrinogen, an acute-phase reactant, increase during an inflammatory response. This soluble protein is involved in platelet aggregation and blood viscosity, and it mediates the final step in clot formation. Significant associations were found between fibrinogen level and risk of cardiovascular events in the Gothenburg, Northwick Park, and Framingham heart studies ***(Lakka et al., 2011).***

7- Other factors

Medical conditions such as end-stage renal disease (ESRD), chronic inflammatory diseases affecting connective tissues (eg, lupus, rheumatoid arthritis), human immunodeficiency virus (HIV)

infection (acquired immunodeficiency syndrome [AIDS], highly active antiretroviral therapy [HAART]), and other markers of inflammation have all been widely reported to contribute to the development of CAD ***(Lakka et al., 2011).***

ESRD is associated with anemia, hyperhomocysteinemia, increased calcium phosphate product, calcium deposits, hypoalbuminemia, increased troponin, increased markers of inflammation, increased oxidant stress, and decreased nitric oxide activity factors, all of which may contribute to increased CAD risk ***(Chiuve et al., 2011).***

The 2010 ACCF/AHA recommendations note that urinalysis to detect microalbuminuria is reasonable for cardiovascular risk assessment in asymptomatic adults with hypertension or diabetes, and might be reasonable for cardiovascular risk assessment in asymptomatic intermediate-risk adults without hypertension or diabetes ***(Greenland et al., 2010).***

Low serum testosterone levels have a significant negative impact on patients with CAD. More studies are needed to assess better treatment. One meta-analysis suggests that the presence of erectile dysfunction increases the risk of cardiovascular disease, coronary heart disease, stroke, and all-cause mortality. This additional risk may be independent of conventional cardiovascular risk factors ***(Chiuve et al., 2011 and Lakka et al., 2011).***

A systemic review and meta-analysis by Cappuccio et al suggests that too little sleep (≤5-6 h per night) or too much sleep (>8-9 h per night) increases risk of coronary heart disease. Too little sleep is also associated with an increased risk of stroke. The association between sleep and cardiac events is consistent across different populations ***(Cappuccio et al., 2000).***

The ACCF/AHA 2010 guideline does not recommend the following measures for coronary heart disease risk assessment in asymptomatic adults:

- Measurement of lipid parameters beyond a standard fasting lipid profile (A standard fasting lipid profile is recommended as part of global risk scoring.)
- Brachial/peripheral arterial flow-mediated dilation studies
- Specific measures of arterial stiffness
- Coronary computed tomography angiography
- MRI for detection of vascular plaque

- ***Ankle-Brachial Index Test***

This test is done by measuring blood pressure at the ankle and in the arm while a person is at rest. Measurements are usually repeated at both sites after 5 minutes of walking on a treadmill. The ankle-brachial index (ABI) result is used to predict the severity of peripheral arterial disease (PAD) ***(Lange et al., 2007).***

A slight drop in your ABI with exercise means that you probably have PAD. This drop may be important, because PAD can be linked to a higher risk of heart attack or stroke ***(Shanmugasundaram et al., 2011).***

Other tests and measures for cardiovascular risk assessment in asymptomatic adults are recommended as reasonable, might be reasonable, or may be considered for specific patient populations and risk levels ***(Bharucha et al., 2000).***

- A resting electrocardiogram (ECG) is reasonable for asymptomatic adults with hypertension or diabetes and may be considered in asymptomatic adults without hypertension or diabetes ***(Lange et al., 2007).***
- An exercise ECG may be considered in intermediate-risk asymptomatic adults (including sedentary adults considering starting a vigorous exercise program), particularly when attention is paid to non-ECG markers such as exercise capacity.
- Transthoracic echocardiography to detect left ventricular hypertrophy may be considered for asymptomatic adults with hypertension but is not recommended in asymptomatic adults without hypertension ***(Huxley et al., 2011).***
- Stress echocardiography is not indicated for low- or intermediate-risk asymptomatic adults.