# INTRODUCTION

Cardiovascular diseases are the leading cause of death worldwide causing about 45.0 million adult deaths worldwide in 2002.Half of such deaths are caused by coronary artery disease (CAD). [1, 2] According to the World Health Organization (WHO), CAD cause 16.7 million deaths in the world each year. [3]

Invasive conventional coronary angiography (CCA) is the gold standard technique for diagnosis and selection of best treatment for CAD. [4]

The detection of cardiac calcification by echocardiography (non- coronary artery calcification) has also been shown to be associated with atherosclerosis, severe coronary artery calcification. It may be of value in the evaluation of patients suspected of having CAD.[5,6]

Using a large echocardiographic database, Mitral annular calcification (MAC) was found to be independently associated with incident CVD, cardiovascular death, and all-cause death. It can be considered as an overall marker of atherosclerotic burden. This finding confirms the importance of an abnormal mitral annulus as an important prognostic marker.[7, 8]

In this study we are going to detect the role of echocardiography calcium score as predictive tool of severity of coronary artery disease in correlation with the

patients' coronary angiography and lipid profile.

# AIM OF WORK

The aim of our study is to determine the correlation of echocardiography calcium score and aortic stiffness to severity of coronary artery disease.

# Chapter one

# ATHEROSCLEROTIC CORONARY ARTERY DISEASE

The 2016 Heart Disease and Stroke Statistics update of the American Heart Association (AHA) reported that 15.5 million persons ≥20 years of age in the USA have coronary artery disease (CAD). This prevalence increases with age for both women and men and it has been estimated that approximately every 42 seconds, an American will suffer for a myocardial infarction (MI).[9]

*1-Epidemiology*

The true frequency of atherosclerosis is very difficult to be accurately determined because it is a predominantly asymptomatic condition. The process of atherosclerosis begins in childhood with the development of fatty streaks in the aorta shortly after birth and increase in those aged 8-18 years. More advanced lesions appear at the age of 25. Subsequently, the prevalence of the advanced complicated lesions of atherosclerosis and the organ-specific clinical manifestations of the disease increase with age through the fifth and sixth decades of life.[10]

Although the absolute numbers of cardiovascular

disease deaths have significantly increased since 1990, the age-standardized death rate has decreased by 22% over the same period mainly due to a shift in age demographics and causes of death worldwide.[11]

MI prevelance was compared by sex in two time periods and found to be higher in men compared with women in the two periods, but it tended to decline in men over time, while the opposite trend was found in women.[12]

For total coronary events, the incidence increases steeply with age, with women lagging behind men.the sex ratio for incidence narrowed progressively with advancing age.[13]

### *2-Pathophysiology*

Previously considered a cholesterol storage disease, we currently understand atherogenesis as a complex interaction of risk factors including cells of the artery wall and the blood and molecular messages that they exchange. Inflammation a major role in all stages of atherogenesis and also participates in the local, myocardial, and systemic complications of atherosclerosis. [14]

Major messages exchanged among the cell types

involved in atherogenesis depend on mediators of inflammation and immunity, including small molecules that include lipid mediators such as prostanoids and other derivatives of arachidonic acid, eg, the leukotrienes. Other autacoids, such as histamine, classically regulate vascular tone and increase vascular permeability. Recently, much attention has focused on protein mediators of inflammation and immunity, including the cytokines and complement components. [15]

Driven by the ascendancy of angiography and the success of revascularization strategies that target arterial stenoses, the degree of arterial narrowing dominated our thinking about the pathophysiology of CAD for decades. We viewed the risk of events as dependent on the degree of stenosis and envisioned atherosclerosis as a segmental or focal disease.[10]

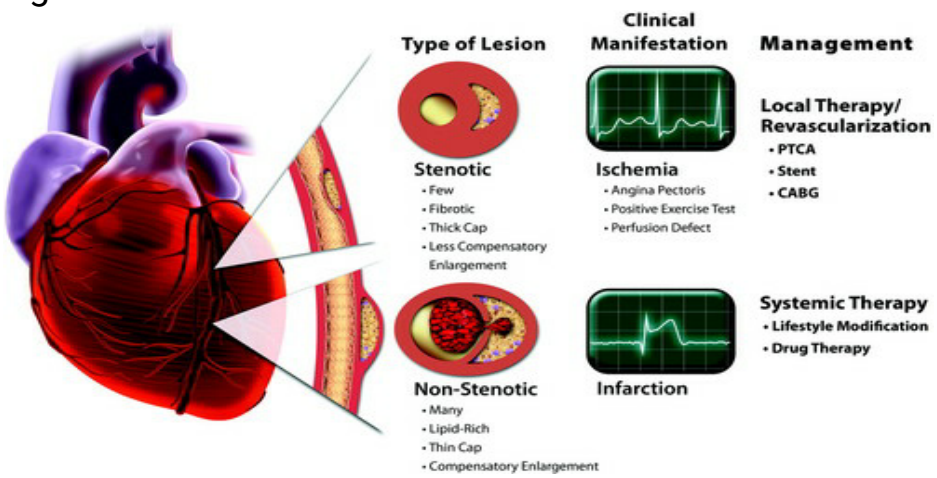


**Figure** (1): Simplified schema of diversity of lesions in human coronary atherosclerosis. 10

There are morphological extremes of coronary atherosclerotic plaques; Stenotic lesions tend to have smaller lipid cores, more fibrosis, and calcification; thick fibrous caps; and less compensatory enlargement (positive remodeling). Nonstenotic lesions generally outnumber stenotic plaques and tend to have large lipid cores and thin, fibrous caps susceptible to rupture and thrombosis. They may cause no symptoms for many years but when disrupted can provoke episode of unstable angina or MI. Many coronary atherosclerotic lesions may lie between these 2 extremes and both types of lesions usually coexist in given high-risk individual, produce mixed clinical manifestations, and require multipronged management.[10]

A new perspective was that, atherosclerotic lesion grows outward, or abluminally, rather than inward. Thus, a substantial burden of atherosclerosis can exist without producing stenosis. Intravascular ultrasound studies have confirmed in vivo older autopsy studies: Stenosis represents the “tip of the iceberg” of atherosclerosis. [16-18]

By the time lesions have progressed to the point of producing stenoses, intimal atherosclerosis usually abounds in a widespread, diffuse distribution. The recognition of the ubiquity of substantial but non–flow-limiting atherosclerotic lesions has considerable consequences for our current understanding of the acute coronary syndromes.[19]

*3-Screening for cardiovascular risk:*

Guidelines on screening for cardiovascular risk, released in late 2013 by the American Heart Association/American College of Cardiology (AHA/ACC),

recommend use of a revised calculator that uses a combination of clinical and laboratory risk factors to estimate risk. The 10-year risk of developing a first atherosclerotic cardiovascular disease (CVD) event is defined as nonfatal MI, death from CAD, or stroke (fatal or nonfatal) in a person who was initially free from atherosclerotic CVD.[20]

For patients 20-79 years of age who do not have existing clinical atherosclerotic CVD, the guidelines recommend assessing clinical risk factors every 4-6 years. For patients with low 10-year risk (< 7.5%), the guidelines recommend assessing 30-year or lifetime risk in patients 20-59 years old.

Regardless of the patient's age, clinicians should communicate risk data to the patient and refer to the AHA/ACC lifestyle guidelines, which cover diet and physical activity. For patients with elevated 10-year risk, clinicians should communicate risk data and refer to the AHA/ACC guidelines on blood cholesterol and obesity.[20]

In 2015, the American College of Physicians (ACP) released guidelines on screening for CAD. There is no evidence that cardiac screening improves patient outcomes in asymptomatic, low-risk adults and may lead to unnecessary tests and procedures. Clinicians should therefore emphasize strategies to reduce cardiovascular

risk even further among low-risk adults by treating modifiable risk factors (smoking, diabetes, blood pressure, hyperlipidemia, overweight, and exercise).The ACP recommendations do not apply to symptomatic patients or to screening athletes before participation in various events.[21]

*4-Approach Considerations:*

*1-Lab Tests:*

Routine blood tests include complete blood count (CBC), chemistry panel, **lipid profile**, and thyroid function tests (to exclude thyroid disorders).1 Routine measurement of blood **glucose** and **hemoglobin** $A_{1c}$is appropriate in patients with diabetes mellitus.[22]

Fasting lipid profile includes; Total cholesterol level, LDL cholesterol (LDL-C) level, HDL cholesterol (HDL-C) level, Triglyceride level and other Specific lipid studies that include; Small, dense LDL-C level, Lipoprotein (a) level, Apoprotein profile and Direct measurement of HDL-C.[10]

C-Reactive Protein (CRP) appears to provide prognostic information for CAD, the CRP assay must be standardized before CRP testing has a clinical benefit. Men with CRP levels in the highest quartile had a 3-fold

greater risk of MI.[23]

*2-Imaging:*

A-functional imaging :

The hallmark of functional imaging is the detection of CAD by assessing the haemodynamic consequences of CAD rather than by direct visualisation of the coronary arteries. For this purpose, regional perfusion or wall motion abnormalities are induced (or worsened) during stress, reflecting the presence of stress induced ischaemia.[24]

Ischaemia induction is based on the principle that although resting myocardial blood flow in regions supplied by stenotic coronary arteries is preserved, the increased flow demand during stress cannot be met, resulting in a sequence of events referred to as “the ischaemic cascade”.[25]

Initially perfusion abnormalities are induced, followed by diastolic and (at a later stage) systolic dysfunction; only at the very end of the cascade do ECG changes and angina occur. Accordingly, the occurrence of perfusion abnormalities during stress may be more sensitive for the detection of CAD than the induction of systolic dysfunction.[25] (figure 2)

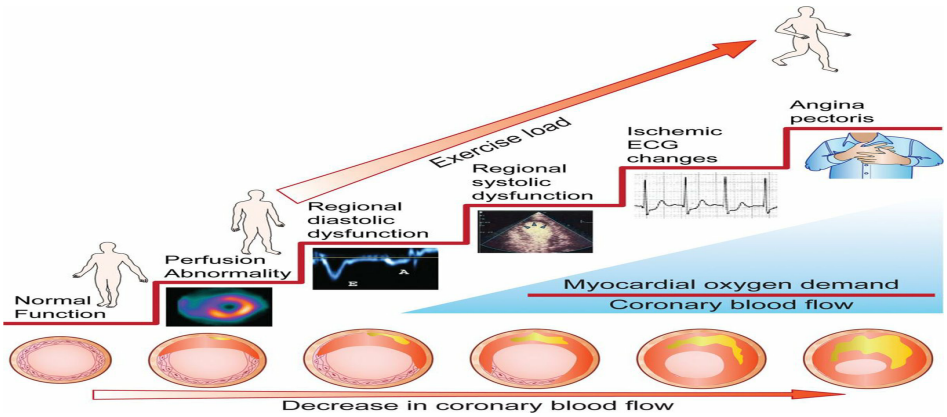


**Figure (2):** Ischemic cascade of coronary artery disease. [26]

*1-SPECT:*

Two sets of images are obtained: after stress and at rest. In general, reversible and irreversible defects are considered indicative of CAD. While reversible (stress induced) defects reflect ischaemia, irreversible (fixed) defects mainly represent infarcted myocardium.[27]

Images are interpreted visually or using automated quantification. For segmentation of the left ventricle (LV), a 17 segment model is developed, that can be applied to all functional imaging modalities.[27] (figures 3,4)

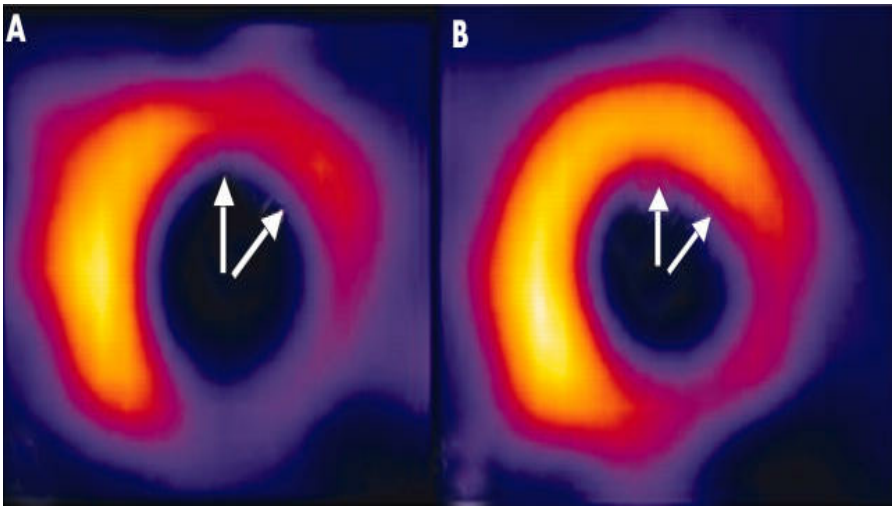


**Figure** (3): Myocardial perfusion defect in tc [99.27]

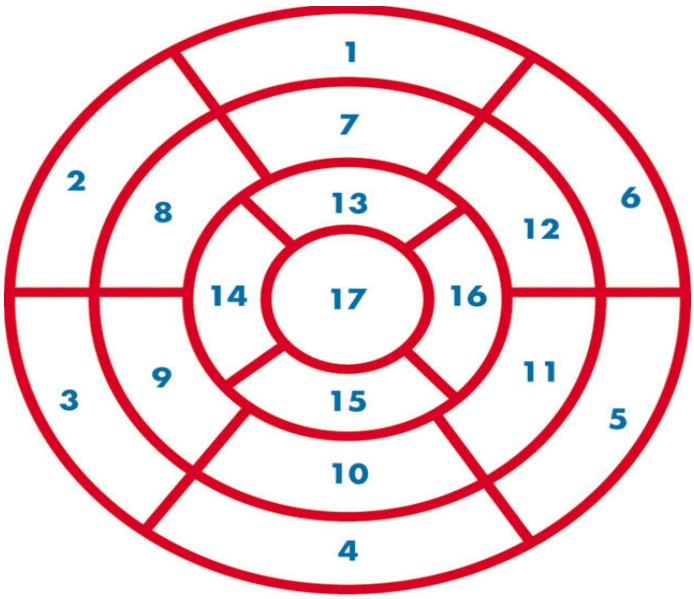


**Figure (4):** the 17 segment model used in stress imaging.[27]

*2-Stress Echocardiography:*

It is used for the routine evaluation of (stress inducible) wall motion abnormalities; both resting and stress induced (or worsened) wall motion abnormalities are indicative of CAD. While stress induced (or worsened) wall motion abnormalities reflect ischemia, resting wall motion abnormalities mainly represent infarcted myocardium. [24] (figure 5)

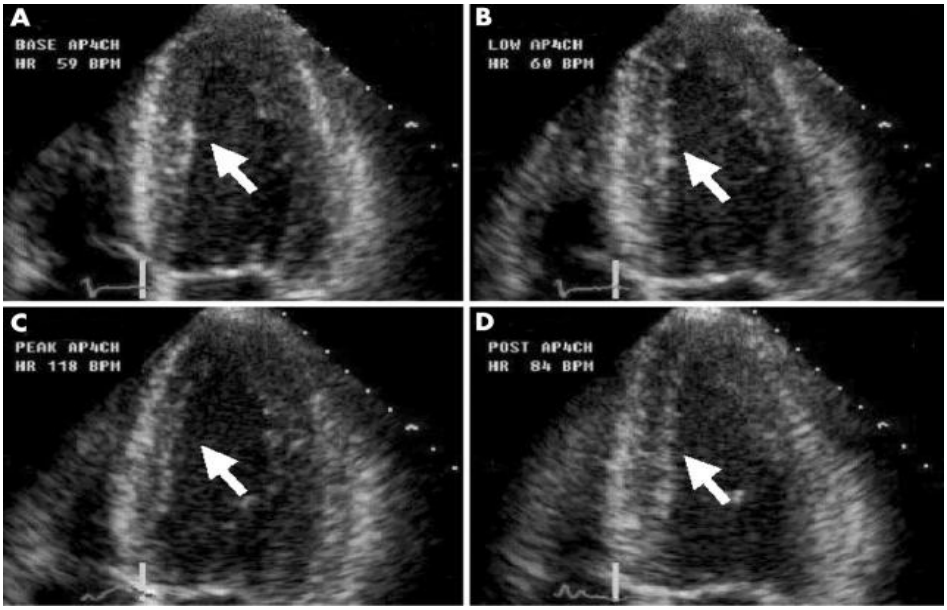


**Figure** (5): SWMA induced with stress echocardiography. [24]

3-MRI:

A relatively new technique to evaluate myocardial perfusion is MRI. For this purpose, 5–8 slices in the short axis orientation are imaged during the first pass of a bolus of a contrast agent. Imaging is repeated during pharmacological stress.[24] (figure 6)

The excellent endocardial blood pool contrast is particularly beneficial for patients with poor echocardiographic windows. Unfortunately, MRI is still limited to highly specialised centres and acquisition protocols are still time consuming, making the technique currently unsuitable for evaluation of larger populations. No MRI studies with integration of systolic wall motion

and perfusion to detect CAD are currently available.[24]

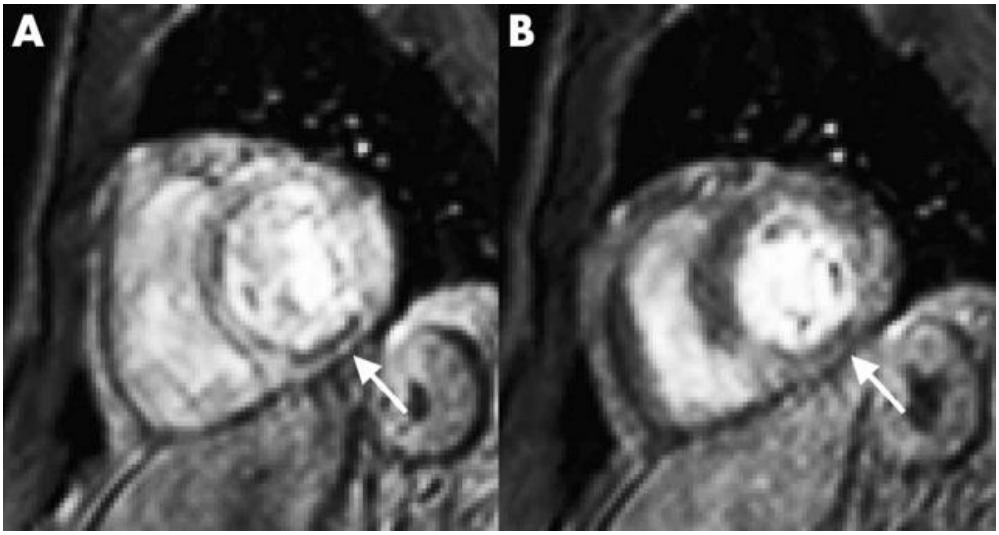


**Figure (6):** MRI imaging with pharmacological stress showing Magnetic resonance perfusion images during rest (panel A) and stress (panel B) showing a fixed perfusion defect in the inferior perfusion defect in the inferior wall (white arrows). [24]

B-Anatomical imaging:

Although a safe and accurate evaluation of patients with known or suspected CAD is offered by functional imaging, in a substantial number of patients anatomical imaging is needed. In patients with abnormal stress tests, direct visualisation of the coronary tree is still required for the definite diagnosis of CAD and decision on treatment strategy.[24]

In other cases diffuse atherosclerosis in all major epicardial vessels is frequently present, resulting in the absence of detectable perfusion abnormalities and