Association of pericardial fat accumulation with coronary atherosclerotic plaque formation in patients with suspected coronary artery disease assessed by Multi-Slice CT

Thesis

Submitted in partial fulfillment of the
Master degree in cardiology

By

Ahmed Said Abdelwahed
M.B.B.CH

Under Supervision of

Mohamed Awad Tahir
Professor of Cardiology
Faculty of Medicine – Ain-Shams University

Khaled Ahmed Fouad
Lecturer of Cardiology
Faculty of Medicine – Ain-Shams University

Faculty of Medicine
Ain-Shams University
٢٠١٣

*I would like to dedicate this thesis to my **sunshine mother** whom I really miss & my **family;** for whom I will never find adequate words to express my gratitude.*

*Also my **Wife** and **beautiful daughter** for making me so patient during this work*

List of Contents

List of Abbreviations

AHA : American heart association
BMI : Body mass index
CABG : Coronary artery bypass graft
CAC : Coronary artery calcium
CAD : Coronary artery disease
CIMT : Carotid intima-media thickness
CT : Computed tomography
CTA : Computed tomography angiography
CVD : Cardiovascular disease
DM : Diabetes mellitus
ECG : Elecrtocardiography
FH : Family history
HDL : High density lipoprotein
HTN : Hypertension
IHD : Ischemic heart disease
IVUS : Intravascular ultrasound
LAD : Left anterior descending artery
LCX : Left circumflex artery
LDL : Low density lipoprotein
LM : Left main artery
MRA : Magnetic resonance angiography
Ms : milli second
MSCT : Multi-Slice computed tomography
NHI : National heart institute
PCI : Percutaneous coronary intervention
PF : Pericardial fat
PFV : Pericardial fat volume
RCA : Right coronary artery
VAT : Visceral adipose tissue

List of Tables

List of Figures

Acknowledgment

First and foremost, I feel always indebted to **Allah**, the most kind and the most merciful.

I would like to express my gratitude to ***Prof. Doctor/ Mohamed Awad Tahir*** *Professor of Cardiology, Faculty of Medicine, Ain-Shams University, for his most valuable advices and support all through the whole work and for dedicating much for his precious time to accomplish this work.*

I am also grateful to ***Doctor/ Khalid Ahmed Fouad,*** *Lecturer of Cardiology, Faculty of Medicine, Ain-Shams University, for his continuous encouragement, supervision and kindness.*

I would like also to thank the whole members of ***cardiology department in Kobry El-Kobba military hospital*** *especially my real teachers* ***Gen.Dr. Sayed Abdelhafiz, Gen.Dr. Alaa Hataba & Gen.Dr.Khalid Shokry*** *and all my colleagues for their true support.*

Introduction

Obesity or excess amount of body fat is a well-established risk factor for coronary heart disease ***(Eckel et al., ١٩٩٨).***

The distribution of body fat varies among individuals and may be as important as the amount of body fat in determining risk. In fact, excess accumulation of fat around the upper body is associated with a higher risk of coronary heart disease regardless of total body fat ***(Rimm et al., ١٩٩٥).***

Waist circumference, reflecting abdominal obesity, is a risk factor of metabolic syndrome and coronary artery disease (CAD). Adipose tissue secretes many factors implicated in atherogenesis; however, the role of pericardial fat (ectopic visceral fat around coronary arteries) in the pathogenesis of CAD is not clear.

Fat depots in various parts of the body have different properties which may underlie the importance of fat distribution. For example, pericardial fat, the fat depot around the heart, releases more inflammatory cytokines than subcutaneous fat ***(Mazurek et al., ٢٠٠٣)***.

Inflammation has been linked to coronary heart disease. Furthermore, inflammation due to fat depots tends to be localized in their surrounding tissues and organs ***(Hansson et al., ٢٠٠٥).***

Therefore, pericardial fat may be the fat depot of principal interest with respect to coronary heart disease.

Multi-slice CT is a noninvasive tool that allows to reliably assessing both obstructive and non-obstructive subclinical coronary artery disease in an earlier stage than invasive angiography ***(Leber et al., ٢٠٠٥)***.

Aim of the Work

The purpose of this study was to examine the association of pericardial fat with the presence of coronary plaques using Multi-Slice CT coronary angiography.

Atherosclerosis

Atherosclerosis is a condition in which an artery wall thickens as a result of the accumulation of fatty materials such as cholesterol. It is a syndrome affecting arterial blood vessels, a chronic inflammatory response in the walls of arteries, caused largely by the accumulation of macrophage white blood cells and promoted by low-density lipoproteins without adequate removal of fats and cholesterol from the macrophages by functional high density lipoproteins (HDL) and resulting in formation of multiple plaques within the arteries ***(Maton et al., ١٩٩٣).***

The atherosclerotic plaque is divided into three distinct components:

١. The atheroma, which is the nodular accumulation of a soft, flaky, yellowish material at the center of large plaques, composed of macrophages nearest the lumen of the artery

٢. Underlying areas of cholesterol crystals

٣. Calcification at the outer base of older/more advanced lesions.

Atherosclerotic plaques are separated into two broad categories: Stable and unstable (vulnerable). Stable atherosclerotic plaques are rich in extracellular and smooth muscle cells, while, unstable plaques are rich in macrophages and foam cells and the extracellular matrix separating the lesion from the arterial lumen

(also known as the fibrous cap) is usually weak and prone to rupture ***(Ross et al., ١٩٩٩)***.

Rupture of the fibrous cap expose thrombogenic material, such as collagen to the circulation and eventually induce thrombus formation in the lumen. Upon formation, intraluminal thrombi can occlude arteries, but more often they detach, move into the circulation and eventually occlude smaller branches causing thromboembolism. Stroke is often caused by thrombus formation in the carotid arteries). Apart from thromboembolism, chronically expanding atherosclerotic lesions can cause complete closure of the lumen. Interestingly, chronically expanding lesions are often asymptomatic until lumen stenosis is so severe that blood supply to downstream tissues is insufficient resulting in ischemia ***(Didangelos et al., ٢٠٠٩).***

These complications of advanced atherosclerosis are chronic, slowly progressive and cumulative. Most commonly, soft plaque suddenly ruptures, causing the thrombus formation that will rapidly stop blood flow, leading to death of the tissues fed by the artery. This catastrophic event is called an infarction. One of the most common recognized scenarios is called coronary artery thrombosis, causing myocardial infarction. The same process in an artery to the brain is commonly called stroke. Another common scenario in very advanced disease is legs claudication, typically caused by a combination of both stenosis and aneurysmal segments narrowed with clots ***(Finn et al., ٢٠١٠).***

Atherosclerosis can occur body-wide, in the arteries to the brain, intestines, kidneys, legs, etc. with many infarctions involving only very small amounts of tissue and termed clinically silent, because the person having the infarction does not notice the problem, does not seek medical help or when they do, physicians do not recognize what has happened ***(Finn et al., ٢٠١٠).***

Causes:

Atherosclerosis develops from low-density lipoprotein molecules (LDL) becoming oxidized by free radicals, particularly reactive oxygen species (ROS). When oxidized LDL comes in contact with an artery wall, a series of reactions occur to repair the artery wall damage caused by oxidized LDL. The body's immune system responds to the artery wall damage caused by oxidized LDL by sending specialized white blood cells (macrophages and T-lymphocytes) to absorb the oxidized-LDL forming specialized foam cells. These white blood cells are unable to process the oxidized-LDL, and ultimately grow then rupture, depositing a greater amount of oxidized cholesterol into the artery wall. This triggers more white blood cells, continuing the cycle. Eventually, the artery becomes inflamed. The cholesterol plaque causes muscle cell enlargement and forms a hard cover over the affected area. This hard cover is what causes arterial narrowing and blood flow reduction (figure ١) ***(Didangelos et al., ٢٠٠٩).***

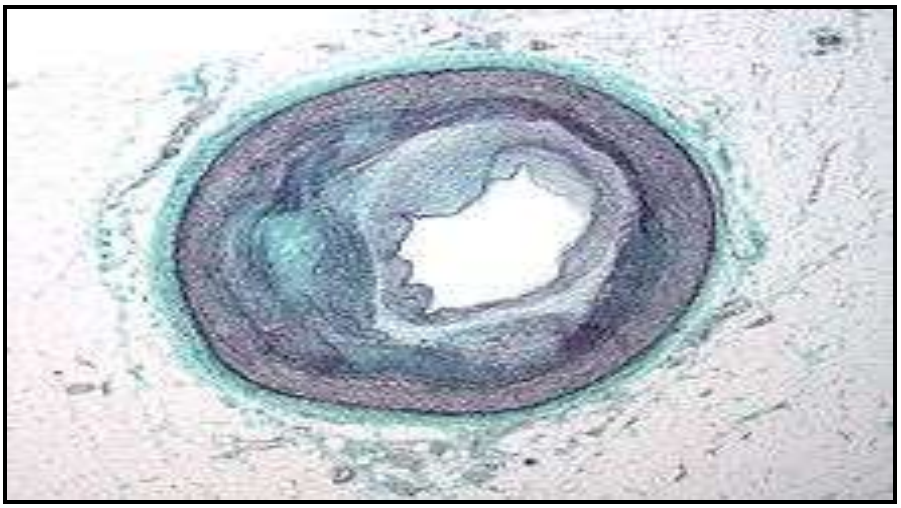

Figure (١): Micrograph of a coronary artery with significant atherosclerosis and marked luminal narrowing. Tissue has been stained using Masson`s trichrome.

Risk factors:

Various anatomic, physiological and behavioral risk factors for atherosclerosis are known. These can be divided into various categories: congenital *vs.* acquired, modifiable or not, classical or non-classical. Risks multiply, with two factors increasing the risk of atherosclerosis fourfold. Hyperlipidemia, hypertension and cigarette smoking together increase the risk seven times ***(Narain et al., ٢٠٠٨).***

Modifiable risk factors:

- Diabetes: defined according to the American heart association **(AHA)** as fasting plasma glucose level of ≥١٢٦ mg/dl or treatment with either insulin or a hypoglycemic agent.
- Hypertension: defined according to the American heart association **(AHA)** as systolic BP > ١٤٠mmHg and/or