Coronary Plaque Characterization of Non Significant Lesions Assessed by Analysis of In-Vivo Intracoronary Ultrasound Virtual Histology

Thesis
Submitted for partial fulfillment of Master degree of Cardiology

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List of Abbreviations

ACS	: Acute Coronary Syndrome
CAFA	: Calcified Fibroatheroma
CATCFA	: Calcified Thin Cap Fibroatheroma
DC	: Dense Calcium
EBCT	: Electron Beam Computed Tomography
EEM	: External Elastic Membrane
FA	: Fibroatheromas
FC	: Fibrocalcific
FF	: Fibrofatty
FI	: Fibrous
FT	: Fibrotic
IDTCFA	: IVUS Derived Thin Cap Fibroatheroma
IMT	: Intimal Medial Thickening
IVUS	: Intravascular Ultrasound
LA	: Luminal Area
LAD	: Left Anterior Descending
LCX	: Left Circumflex
LD MAX	: Maximal Luminal Diameter
LD MIN	: Minimal Luminal Diameter
LM	: Left Main
MDCT	: Multi Detector Computed Tomography
MLA	: Minimal Lumen Area
MRI	: Magnetic Resonance Imaging
NC	: Necrotic Core
NIR	: Near Infra Red
OCT	: Optical Coherence Tomography
PIT	: Pathological Intimal Thickening
RCA	: Right Coronary Artery
RI	: Remodeling Index
TCFA	: Thin-Cap Fibroatheromas
VH	: Virtual Histology

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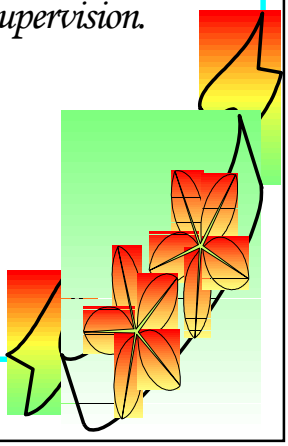

Introduction

Acute coronary syndrome (ACS) is common initial manifestation of coronary atherosclerosis and most of such events arise from sites with non-flow limiting coronary atherosclerosis[1].

Histopathological studies have suggested that plaque composition is a crucial determinant of the propensity of atherosclerotic lesions to rupture[2].

Coronary artery lesions with a thin fibrous cap and large necrotic core (thin-cap fibroatheromas, TCFA) are characterized by a high risk of rupture and can potentially trigger acute coronary syndrome (ACS) while atherosclerotic lesions with a well preserved fibrous cap (fibroatheromas, FA) are considered to be more stable ones[3].

Detection of these non-obstructive, lipid rich, high-risk plaques may have an important impact on the prevention of acute myocardial infarction and sudden death[2].

Intravascular ultrasound (IVUS) is the golden standard for evaluation of coronary plaque, lumen, and vessel dimensions[4].

Visual interpretation of gray-scale IVUS can identify calcification within plaques; but it cannot reliably differentiate lipid-rich from fibrous plaque[4].

Spectral analysis of IVUS radiofrequency data (IVUS-Virtual histology) demonstrated its potential to assess coronary

plaque composition objectively and accurately[5], Whether FA or TCFA in vivo[3].

IVUS-VH (Intravascular ultrasound-Virtual histology) uses spectral analysis of IVUS radiofrequency data to build tissue maps that are correlated with a specific spectrum of the radiofrequency signal and assigned color codes (fibrosis (labeled green), fibrofatty (labeled greenish-yellow), necrotic core (labeled red) and calcium (labeled white))[5].

Aim of The Work

This study aims to assess IVUS-VH plaque characteristics of angiographically non-significant lesions in patients with history of ischemic heart disease either with ACS or with stable angina pectoris.

Chapter 1

Coronary Plaque Development and Plaque Vulnerability

Introduction:

Cardiovascular disease is the leading cause of death for both men and women and is predicted to be the leading global killer by 2020[6].

Atherosclerosis is a disease of large and medium-sized muscular arteries and is characterized by endothelial dysfunction, vascular inflammation, and the buildup of lipids, cholesterol, calcium, and cellular debris within the intima of the vessel wall. This buildup results in plaque formation, vascular remodeling, acute and chronic luminal obstruction, abnormalities of blood flow and diminished oxygen supply to target organs [7].

Pathophysiology:

The mechanisms of atherogenesis remain uncertain. The "response-to-injury" theory is the most widely accepted one. Endothelial injury causes vascular inflammation and a fibroproliferative response ensues. Endothelial injury is caused by oxidized low-density lipoprotein (LDL) cholesterol; infectious agents; toxins, including the byproducts of cigarette smoking; hyperglycemia; and hyperhomocystinemia [7].

Then circulating monocytes infiltrate the intima of the vessel wall, and these tissue macrophages act as scavenger

cells, taking up LDL cholesterol and forming the characteristic foam cell of early atherosclerosis. These activated macrophages produce numerous factors that are injurious to the endothelium [7].

The earliest pathologic lesion of atherosclerosis is the fatty streak. The fatty streak is observed in the aorta and coronary arteries of most individuals by age 20 years. Histologic and intravascular ultrasound studies have shown that coronary lesion development starts relatively early in life [8].

The fatty streak may progress to form a fibrous plaque, the result of progressive lipid accumulation and the migration and proliferation of smooth muscle cells. Platelet-derived growth factor, insulin-like growth factor, transforming growth factors alpha and beta, thrombin, and angiotensin II are potent mitogens that are produced by activated platelets, macrophages, and dysfunctional endothelial cells[7].

These smooth muscle cells are responsible for the deposition of extracellular connective tissue matrix and form a fibrous cap that overlies a core of lipid-laden foam cells, extracellular lipid, and necrotic cellular debris. The developing atherosclerotic plaques acquire their own microvascular network called vasa vasorum, which are prone to hemorrhage and contribute to progression of atherosclerosis[7].

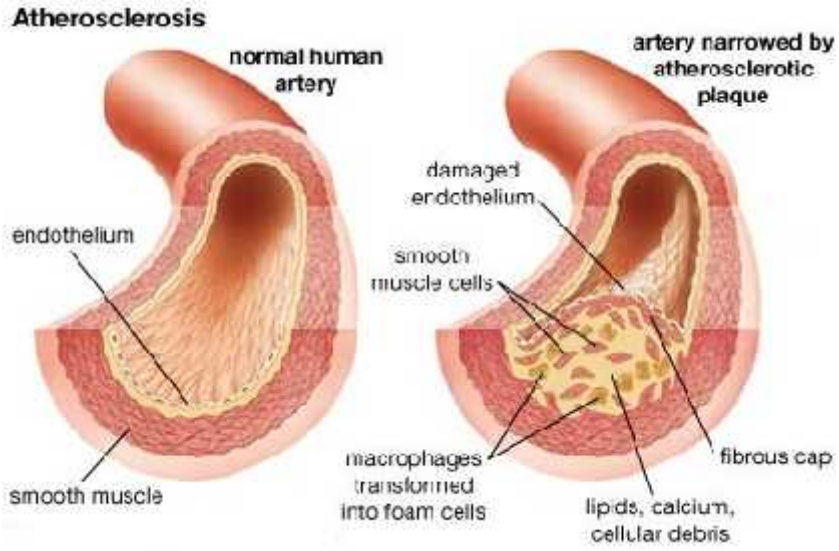

Figure1: Coronary plaque formation [9].

Fissure or rupture of the fibrous cap is the underlying basis for 70 to 80% of coronary thrombi with extension of the thrombus into the plaque as well as into the lumen, and with propagation of the thrombus upstream from the site of cap rupture[10].

Plaque vulnerability:

Originally proposed by Muller and Tofler in 1992, the term vulnerable plaque (VP) was redefined as any atherosclerotic lesion subsequently resulting in coronary thrombosis [11].

Three forms of vulnerable plaques were described: Thin cap fibroatheroma, erosion, and calcified nodules.

a) Thin cap fibroatheroma

Pathologic studies of plaque rupture with thrombosis suggest that prior to a thrombotic event; a plaque is an