

**The Relation Between Neutrophil /Lymphocyte
Ratio and Atherosclerotic Coronary Artery
Disease Detected by Multislice Computed
Tomography in Type Two Diabetic Patients**

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سببناك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

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List of Abbreviations

Abb.	Full term
AAA.....	<i>Abdominal aortic aneurysm</i>
ABOS.....	<i>Atheroma burden obstructive score</i>
ACS.....	<i>Acute coronary syndrome</i>
AF.....	<i>Atrial fibrillation</i>
AGN.....	<i>Angio-negative</i>
AGP.....	<i>Angio-positive</i>
ANOVA.....	<i>Analysis of variance</i>
ASSH.....	<i>Ain Shams Specialized Hospital</i>
CABG.....	<i>Coronary artery bypass grafting</i>
CAC.....	<i>Coronary artery calcium</i>
CACS.....	<i>Coronary artery calcium score</i>
CAD.....	<i>Coronary artery disease</i>
CI.....	<i>Confidence interval</i>
cMPR.....	<i>Curved multiplanar reformation</i>
CRP.....	<i>C- reactive protein</i>
CT.....	<i>Computed tomography</i>
CTDI.....	<i>Computed tomography dose index</i>
CVD.....	<i>Cerebrovascular disease</i>
EC.....	<i>Endothelial cell</i>
ECG.....	<i>Electrocardiogram</i>
FDA.....	<i>United States Food and Drug Administration</i>
FOV.....	<i>Field of view</i>
Hb.....	<i>Hemoglobin</i>
Hct.....	<i>Hematocrit</i>
HDL.....	<i>High density lipoprotein</i>
HR.....	<i>Hazard ratio</i>
ICAM.....	<i>Intercellular adhesion molecule</i>
IHD.....	<i>Ischemic heart disease</i>
kVp.....	<i>Kilovoltage peak</i>
LA.....	<i>Left atrium</i>

List of Abbreviations Cont...

Abb.	Full term
<i>LAD</i>	<i>Left anterior descending artery</i>
<i>LCx</i>	<i>Left circumflex artery</i>
<i>LDL</i>	<i>Low density lipoprotein</i>
<i>LDL-C</i>	<i>Low density lipoprotein cholesterol</i>
<i>LMCA</i>	<i>Left main coronary artery</i>
<i>Lp (a)</i>	<i>Lipoprotein a</i>
<i>LV</i>	<i>Left ventricle</i>
<i>mA</i>	<i>Millamperes</i>
<i>MACE</i>	<i>Major adverse cardiac events</i>
<i>MCH</i>	<i>Mean corpuscular hemoglobin</i>
<i>MCHC</i>	<i>Mean corpuscular hemoglobin concentration</i>
<i>MCP</i>	<i>Monocytes chemoattractant protein</i>
<i>MCV</i>	<i>Mean corpuscular volume</i>
<i>mGy • cm</i>	<i>Milligray- centimeter</i>
<i>MI</i>	<i>Myocardial infarction</i>
<i>MIP</i>	<i>Maximum-intensity projection</i>
<i>MPR</i>	<i>Multiplanar reformat</i>
<i>MSCT</i>	<i>Multisclice computed tomography</i>
<i>MUST</i>	<i>Misr University for science and technology</i>
<i>NLR</i>	<i>Neutrophil-to-Lymphocyte Ratio</i>
<i>NO</i>	<i>Nitric oxide</i>
<i>OM</i>	<i>Obtuse marginal</i>
<i>PAD</i>	<i>Peripheral artery disease</i>
<i>PAMP</i>	<i>Pathogen –associated molecular pattern</i>
<i>Pc</i>	<i>Pericardium</i>
<i>PCI</i>	<i>Percutaneous coronary intervention</i>
<i>PCSK9</i>	<i>Proprotein convertase inhibitor subtilisin/ kexin type 9</i>
<i>RA</i>	<i>Right atrium</i>

List of Abbreviations Cont...

Abb.	Full term
<i>RCA</i>	<i>Right coronary artery</i>
<i>RCT</i>	<i>Randomized controlled trial</i>
<i>RDW</i>	<i>Red blood cell distribution width</i>
<i>RV</i>	<i>Right ventricle</i>
<i>S.D</i>	<i>Standard deviation</i>
<i>ScR</i>	<i>Scavenger receptor</i>
<i>SIS</i>	<i>Segment involvement score</i>
<i>SMC</i>	<i>Smooth muscle cell</i>
<i>SPSS</i>	<i>Statistical package for social sciences</i>
<i>SSS</i>	<i>Segment stenosis score</i>
<i>Sv</i>	<i>Sievert</i>
<i>SYNTAX</i>	<i>SYNergy between PCI with TAXus and cardiac surgery</i>
<i>T h</i>	<i>T helper subtype</i>
<i>T2DM</i>	<i>Type 2 diabetes mellitus</i>
<i>TGF-β</i>	<i>Transforming growth factor –beta</i>
<i>TLC</i>	<i>Total leucocytic count</i>
<i>TLRs</i>	<i>Toll-like receptors</i>
<i>Treg</i>	<i>Regulatory T cells</i>
<i>VCAM</i>	<i>Vascular cell adhesion molecule</i>
<i>VR</i>	<i>Volume-rendered</i>
<i>VTE</i>	<i>Venous thromboembolism</i>
<i>WBC</i>	<i>White blood cell</i>

INTRODUCTION

The term atherosclerosis is derived from the Greek words “Athero” meaning gruel and “Sclerosis” meaning hardening. It is an inflammatory fibroproliferative response to retention of atherogenic lipoproteins in the arterial intima.

It is the most important cause of mortality worldwide.^{1,2} In USA: CAD accounting for >400,000 deaths annually. About 785,000 Americans have an initial AMI and about 470,000 have a recurrent attack.¹ In Egypt: overall prevalence of CAD is 8.3%. CAD is more in women than in men (8.9% vs. 8%), more in urban than in rural areas (8.2% vs. 7.2%) and age >50 years vs. <50 years (11.1% vs. 5.1%). High prevalence of hypertension in Egypt was the most important risk factor of adverse cardiovascular outcomes.^{3,4}

Evidence has demonstrated important role of inflammation in atherosclerosis. The macrophage foam cells are a rich source of proinflammatory mediators and elaborate large quantities of oxidant species. This can promote inflammation in the plaque and progression of the lesion i.e. “innate immunity”. There is also an important role of antigen specific or adaptive immunity in plaque progression. Dendritic cells in the lesion can present antigens to the T cells. Antigens include modified or native lipoproteins, heat shock proteins B2, glycoprotein Ib, and infectious agents. Active T cells then secrete large amount of cytokines. The helper T cells have 2

categories, T helper 1 elaborate proinflammatory cytokines and T helper 2 can inhibit inflammation.⁵⁻⁸

Risk factors for CAD include older age, hypertension, D.M., smoking, obesity, lack of physical activity, mental stress and family history of premature coronary artery disease are also considered risk factors for coronary artery diseases. There are novel risk factors such as high CRP level, lipoprotein (a) and homocysteine.

Diabetic patients who have developed cardiac dysfunction have several molecular signaling pathways that were broken. The disorder of oxidative metabolism increases free fatty acids circulation and lipid metabolism, and this process ends up with lipid accumulation.⁹

Multislice computed tomography coronary angiography (MSCT-CA) is an emerging modality in detection and classification of ischemic heart disease.¹⁰

AIM OF THE WORK

The aim is to investigate the association of neutrophil /lymphocyte ratio (NLR) and atherosclerotic coronary artery disease (CAD) detected by multislice computed tomography (MSCT) coronary angiography in type two diabetic (T2DM) patients.

Chapter 1

ATHEROSCLEROSIS

Structure of the normal artery:

Cell types composing the normal artery:

Endothelial Cells:

The endothelial cell (EC) of the arterial intima constitutes an important contact surface with blood. It plays an important role in vascular homeostasis. This blood compatibility is due to presence of heparan sulfate proteoglycan molecules on the surface of the EC. These molecules can serve as a cofactor for antithrombin III, which inhibit thrombin. The surface of the EC also contains thrombomodulin which activates protein C and S. Also, the EC can produce tissue- and urokinase- type plasminogen activators which activate plasminogen into plasmin. (Fig.1) ECs are originated from a common origin known as blood islands in the embryo's periphery.⁵

Arterial Smooth muscle cells:

Smooth muscle cell (SMC) is the second major cell type of the normal artery. These cells contract and relax thus controlling blood flow through various arterial beds. These cells can migrate and proliferate leading to formation of hyperplastic lesions. Death of these smooth muscle cells causes destabilization of the atheromatous plaques or may lead to ectatic remodeling and aneurysm formation. Unlike ECs, SMCs can arise from many

sources. (Fig.2) In the descending aorta, the regional mesoderm serves as the source of smooth muscle precursors. In arteries of the upper body, SMCs are derived from neurectoderm. The coronary artery SMCs arise from the proepicardial organ.¹²

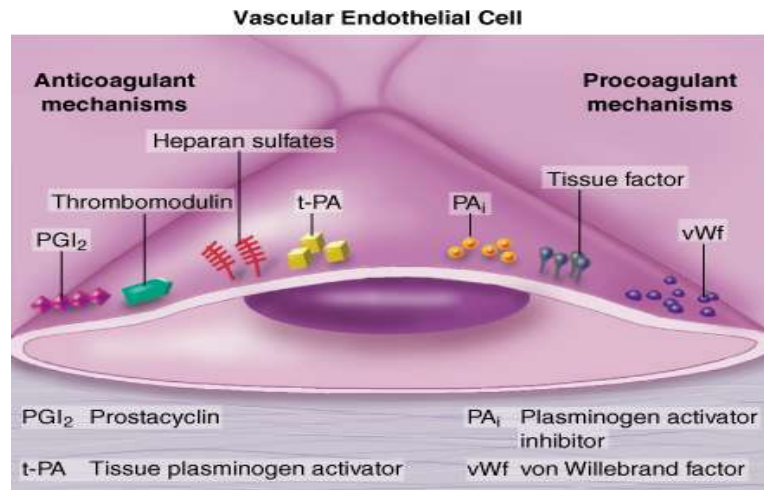


Fig. (1): The endothelial thrombotic balance.⁵

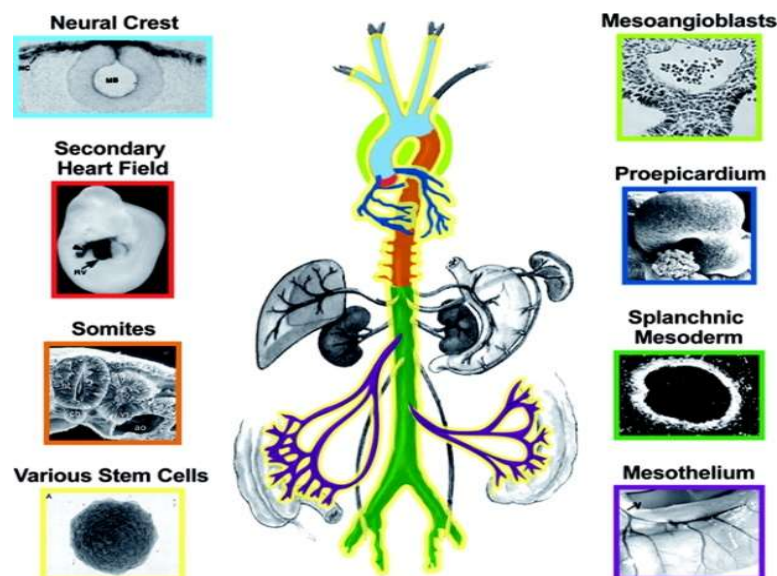


Fig. (2): Embryologic origin of vascular SMCs.¹²