Absolute Eosinophilic Count & Eosinophil Leucocyte Ratio in Acute Coronary Syndrome

Thesis

Submitted for Partial Fulfillment
of Master Degree in **Cardiology**

By

Mina Tuodor Wadie
M.B.B.Ch, Ain Shams University

Under Supervision of

Prof. Dr. Mohammed Tarek Mounir Zaki
Professor of Cardiology
Faculty of Medicine, Ain Shams University

Dr. John Kamel Zarif
Lecturer of Cardiology
Faculty of Medicine, Ain Shams University

Dr. Islam Mahmoud Bastawy
Lecturer of Cardiology
Faculty of Medicine, Ain Shams University

Faculty of Medicine, Ain Shams University
2018

Acknowledgments

First and foremost, I feel always indebted to ***Allah*** *the Most Beneficent and Merciful.*

I wish to express my deepest thanks, gratitude and appreciation to ***Prof. Dr. Mohammed Tarek Mounir Zaki****, Professor of Cardiology, Faculty of Medicine, Ain Shams University, for his meticulous supervision, kind guidance, valuable instructions and generous help.*

Special thanks are due to ***Dr. John Kamel Zarif****, Lecturer of Cardiology, Faculty of Medicine, Ain Shams University, for his sincere efforts, fruitful encouragement.*

I am deeply thankful to ***Dr. Islam Mahmoud Bastawy****, Lecturer of Cardiology, Faculty of Medicine, Ain Shams University, for his great help, outstanding support, active participation and guidance.*

I would like to express my hearty thanks to all my family for their support till this work was completed.

Mina Tuodor Wadie

List of Contents

List of Tables

Table No.	Title	Page No.

List of Figures

List of Figures cont...

List of Abbreviations

Abb.	Full term
ACS	*Acute coronary syndrome*
ESR	*Erytherocyte sedimentation rate*
HTN	*Hypertension*
IHD	*Ischemic heart disease*
Non STEMI	*Non ST elevation myocardial infarction*
STEMI	*ST elevation myocardial infarction*
UA	*Unstable angina*

Introduction

Cardiovascular diseases continue to be significant causes of mortality and morbidity in the Western world. Although in the past atherosclerosis was considered to be the result of passive lipid accumulation in the vessel wall [1]. Today it is considered as chronic inflammatory disease that results in the formation of plaques that can erode or rupture, leading to acute coronary events. [2]

Inflammation plays an important role in the development of atherosclerosis, which can lead to acute myocardial infarction and is also a key factor in the long-term outcome of acute coronary syndrome (ACS). Cells of the innate and adaptive immune system play a crucial role in pathogenesis of atherosclerosis. Immune cells are present in early atherosclerotic lesions and release effector substances that accelerate the progression of lesions and induce activation of inflammation that can elicit (ACS). [3]

Since inflammation plays a key role in atherosclerosis, discovering new biomarkers of inflammation becomes important in order to help diagnostic accuracy and to provide prognostic information about this disease. This will help clinicians in deciding how aggressively they need to treat such diseases. [4]

The role of total white blood cell count in patients with acute myocardial infarction has been emphasized in several studies. Leukocytes are major mediators of inflammation and have a key role in host defense to injury. Increased white blood cell count has been associated with a worse outcome in patients with stable coronary disease, in acute coronary syndromes, and even in general population. [5]

These cells may act through several mechanisms including the production of rheologic compromise of the microvasculature by adhesion, aggregation, platelet recruitment, distal embolization, microvascular plugging, and microvasculature obstruction. They can form platelet–leukocyte aggregate, provide catalytic surface for thrombin generation, and produce tissue factor thus facilitating thrombosis and acute coronary events. [6]

Eosinophils are multifunctional leukocytes implicated in the pathogenesis of numerous inflammatory processes including allergic diseases, tumor immunity, tissue injury, bacterial infections, viral infections and parasitic helminthes. Eosinophils are recruited from the circulation into inflammatory sites where they modulate immune responses through an array of mechanisms [7]. Their surface brings H4 histamine receptors that facilitate eosinophil chemostaxis toward mast cells, which are the major producers of an array of inflammatory soluble mediators. Soluble mediators secreted by mast cells and eosinophils also modulate reciprocal interactions between these 2 cells in the so-called ‘‘allergic effector unit.’’ [8] Several studies have shown the role of eosnophils as a novel biomarker for risk stratification of patients with coronary artery disease. [9]

Aim of the Work

In this study we will compare the changes in absolute eosinophilic count and eosinophil leucocytic ratio in patients with acute coronary syndrome and general population.

Acute Coronary Syndrome & Inflammatory Process

ACS are life-threatening disorders that remain a source of high morbidity and mortality despite advances in treatment. Nearly 1.5 million hospital discharges involve patients with ACS. According to statistics from the American Heart Association (AHA), approximately 18% of men and 23% of women over the age of 40 will die within 1 year of having an initial recognized myocardial infarction (MI). [10]

(ACS) refers to any condition attributed to obstruction of the coronary arteries which reduces blood flow to the heart, and includes unstable angina and myocardial infarction (MI).

Although it is not included under the umbrella of ACS, stable angina is categorised within ischaemic heart disease. Temporary discomfort occurs from a chronic flow limiting lesion within a coronary artery and occurs when the demand for blood supplied to the myocardium is increased, for example during physical exertion or emotional stress.

Clinical presentation, clinical history, electrocardiogram (ECG) and biomarkers are used to define ACS as follows which is summarised in the figure below.

ST elevation myocardial infarction (STEMI) refers to ST segment elevation on a patient's ECG who generally have

cardiac biomarkers (i.e., elevated troponin level), which indicate necrosis of heart muscle. The pathway for clinical management focuses on early reperfusion therapy either by thrombolytic therapy or revascularisation with Percutaneous coronary intervention (PCI).

- *Non ST segment elevation acute coronary syndrome (NSTEACS)* refers to symptomatic individuals whose first ECG shows no ST elevation. Risk stratification occurs until a diagnosis of NSTEMI or unstable angina is made. These patients are stratified as low, intermediate or high risk in terms of adverse outcome.

- *Non ST elevation myocardial infarction (NSTEMI)* refers to those people who have not had ST elevation on their ECG, however, subsequent cardiac biomarkers are elevated. Up to 50% of patients diagnosed as NSTEMI have an ECG that is normal or only show minor changes.

- *Unstable angina* is an accelerated pattern of angina with or without ECG changes. It is distinguished from NSTEMI by the absence of elevated cardiac biomarkers.

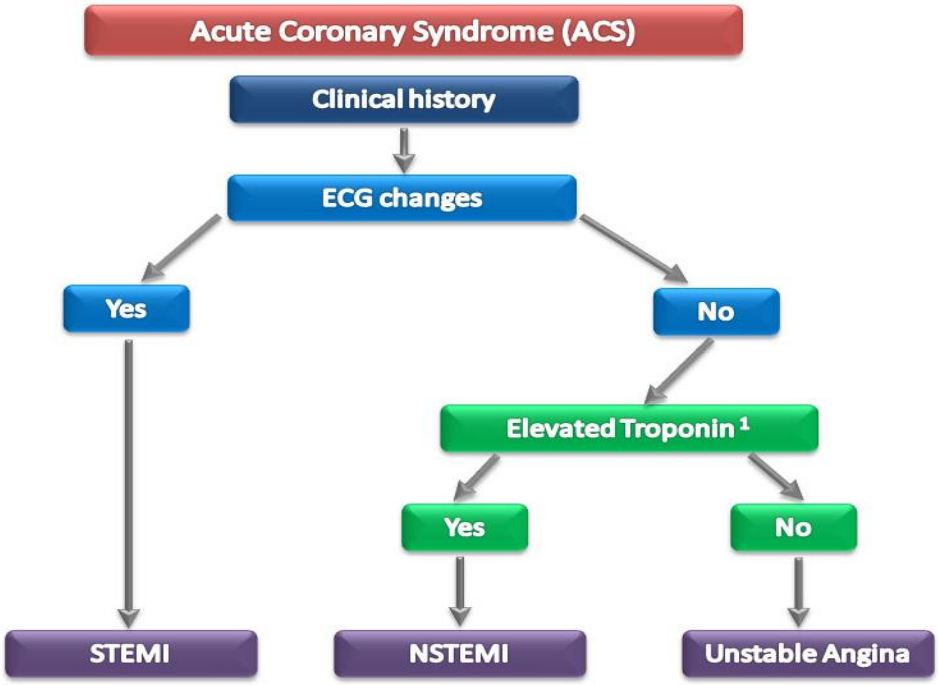

Figure 1: Acute coronary syndrome (ACS).

Atherosclerosis and its consequences, coronary artery disease and MI, continue to be significant causes of mortality and morbidity in the Western world.[3] Recent research has shown that immune cells are present in early atherosclerotic lesions and release effector substances that accelerate the progression of lesions and induce activation of inflammation that can elicit ACS. Since inflammation plays a key role in atherosclerosis and its end results coronary artery disease, angina pectoris, and MI, discovering new biomarkers of inflammation becomes important in order to help diagnostic accuracy and to provide prognostic information about this disease. [12]

Acute-phase protein markers	Serum C-reactive protein, pentraxin 3, amyloid A, homocysteine, fibrinogen
Blood cells	Erythrocyte sedimentation rate, monocytes, soluble CD40 ligand, leukocytes, neutrophils, neutrophil–leukocyte ratio, neutrophil–lymphocyte ratio, eosinophil, eosinophil–leukocyte ratio
Biomarkers of plaque instability	Myeloperoxidase, myeloid-related protein 8/14, pregnancy-associated plasma protein A (PAPP-A), C-reactive protein
Proinflammatory cytokine markers	Interleukins 6, 10, 13, 17, 18, 27, 33, tumor necrosis factor α, soluble ST2, interleukin 1 receptor antagonist, transforming growth factor β receptor 1
Substances involved in lipid metabolism	Lipoprotein-associated phospholipase A2, lysophosphatidylcholine, galectin 3

Figure 2: Biomarkers of inflammation.

Atherosclerosis as Inflammatory Process

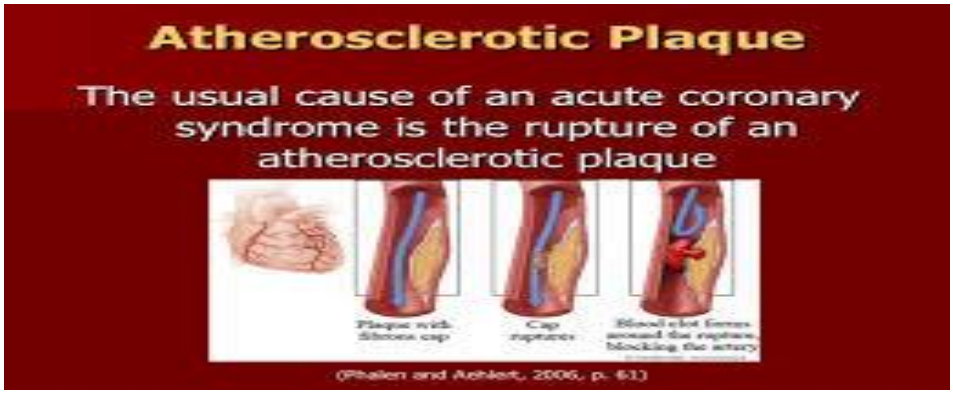

Figure 3: Atherosclerotic plaque.

Inflammation plays an important role in the development of atherosclerosis, which can lead to acute MI and is also a key factor in the long-term outcome of ACS. Although in the past atherosclerosis was considered to be the result of passive lipid accumulation in the vessel wall, today it is considered as chronic inflammatory disease that results in the formation of plaques that can erode or rupture, leading to acute coronary events. Cells of the innate and adaptive immune system play a crucial role in pathogenesis of atherosclerosis. The immune

system decisively influences the propensity of a given plaque to rupture and cause clinical symptoms such as cardiovascular and cerebrovascular events. This takes place via transformation of immune cells into pro- and anti-inflammatory chemokine- and cytokine-producing units and by guiding the interactions between the different immune cells. The inflammatory activity within the atherosclerotic plaques may be detected by markers of inflammation that have been found to be associated with both extent and severity of atherosclerotic lesions. In an effort to predict single or repeated ischemic episodes of NSTEMI, STEMI, UA and numerous such markers have been proposed. However, the knowledge that atherosclerosis is an inflammatory disease offers new opportunities for the prevention and treatment of coronary artery disease, and in this extend, the discovery of new biomarkers of inflammation is of paramount importance.

There is substantial evidence implicating an inflammatory process in the pathogenesis of ACS. Local inflammatory cells can generate and release cytokines that have the potential to activate the endothelium, transforming its natural antiadhesive and anticoagulant properties. Furthermore, inflammatory cytokines may reduce matrix synthesis and increase its degradation, favouring plaque rupture. Finally, cytokines may enhance synthesis of endothelin in endothelial cells and macrophages, resulting in increased smooth muscle cell reactivity to local vasoconstrictors. The evidence