بسم الله الرحمن الرحيم

شبكة المعلومـــــات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

﴿ قـــسـم ﴾

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأفلام قد اعدت دون آية تغيرات

يجب أن

تحفظ هذه الأفلام بعيداً عن الغبار

في درجة حرارة من 15 – 20 مئوية ورطوبة نسبية من 20-40 %

To be kept away from dust in dry cool place of
15 – 25c and relative humidity 20-40 %

بعض الوثائق الأصلية تالفة

بالرسالة صفحات

لم ترد بالأصـــل

SHORT TERM PROGNOSTIC VALUE OF TROPONIN AND C-REACTIVE PROTEIN IN PATIENTS WITH UNSTABLE ANGINA PECTORIS

THESIS

Submitted to the Faculty of Medicine
University of Alexandria
in partial fulfilment of the requirements for

Master Degree

of

Critical Care Medicine

By

AYMAN MOHAMED NAZMY BADAWY

MBBCh, Alex.

Faculty of Medicine
Alexandria University
2002

SUPERVISORS

Prof. Dr. MOHAMED AHMED SOBHY

Professor of Cardiology

Faculty of Medicine

University of Alexandria

Dr. AMR MAHMOUD NAEEM

Assistant Professor of Cardiology

Faculty of Medicine

University of Alexandria

Dr. NABIL AHMED KAMAL

Fellow of Critical Care Medicine

Critical Care Department

Faculty of Medicine

University of Alexandria

ACKNOWLEDGMENT

Thanks God, for everything done in this work.

It is great honour to express my deepest gratitude and cordial appreciation to Prof. Dr. ***MOHAMED AHMED SOBHY,*** *Professor of Cardiology, Faculty of Medicine, University of Alexandria for his meticulous supervision, constant guidance and encouragement. He did every effort and spared no time to offer his help up to the utmost.*

I also thank Dr. ***AMR MAHMOUD NAEEM,*** *Assistant Professor of Cardiology, Faculty of Medicine, University of Alexandria for his valuable suggestions, encouragement and supervision all over the course of this work.*

I would like to express my great appreciation and thanks to Dr ***NABIL AHMED KAMAL,*** *Fellow of Critical Care Medicine, Critical Care Department, Faculty of Medicine, University of Alexandria, for his sincere cooperation and the lot of time he spent sharing in this work.*

Finally, my great appreciation is given to all those who shared either practically or morally in the creation of this work.

CONTENTS

CHAPTER		PAGE
I	INTRODUCTION	1
II	AIM OF THE WORK	28
III	PATIENTS	29
IV	METHODS	30
V	RESULTS	36
VI	DISCUSSION	57
VII	SUMMARY	67
VIII	CONCLUSIONS	69
IX	RECOMMENDATION	70
X	REFERENCES	71
	PROTOCOL	
	ARABIC SUMMARY	

INTRODUCTION

INTRODUCTION

Unstable angina lies in the center of the spectrum of clinical conditions caused by myocardial ischemia. These range from chronic stable angina to acute coronary syndromes. The latter in term consist of acute myocardial infarction associated with ST segment elevation (STEMI), unstable angina (UN), and non ST segment elevation myocardial infarction (NSTEMI).

DEFINITION:

Unstable angina is defined as angina pectoris or equivalent type of ischemic discomfort with at least one of these features (1) it occurs at rest or with minimal exertion usually lasting more than 20minutes (if not interrupted by nitroglycerin intake); (2) it is severe and described as frank pain and of new onset (i.e., within one month); and (3) it occurs with a crescendo pattern (i.e., more severe, prolonged, or frequent than previous). [1]

CLASSIFICATION :

Because unstable angina comprises such a heterogeneous group of patients, classification schemes based on clinical features have been proposed.

Braunwald classification of unstable angina divides patients into three groups according to the clinical circumstances of the acute ischemic episode: primary unstable angina, secondary unstable angina, and post-myocardial infarction unstable angina. Patients are also classified

according to the severity of the ischemia (acute rest pain, subacute rest pain, or new-onset severe angina).

TABLE 1. BRAUNWALD CLASSIFICATION OF UNSTABLE ANGINA [2]

CLASS	DEFINITION
severity	
CLASS I	New onset of severe angina or accelerated angina; no chest pain
CLASS II	Angina at rest within past month but not within preceding 48 hr
CLASS III	Angina at rest within 48 hr
clinical circumstances	
A (secondary angina)	Develops in the presence of extracardiac condition that intensifies myocardial ischemia
B (primary angina)	Develops in the absence of extracardiac condition
C (postinfarction angina)	Develops within 2 weeks after acute myocardial infarction
Intensity of treatment	Patients with unstable angina may also be divided into three groups depending on whether unstable angina occurs (1) in the absence of treatment for chronic stable angina, (2) during treatment for chronic stable angina, or (3) despite maximal antiischemic drug therapy. The three groups may be designated subscripts 1, 2, or 3, respectively.
ECG changes	Patients with unstable angina may be further divided into those with or without transient ST-T wave changes during pain.

This classification has been shown to be predictive of plaques with thrombus at angiography. [3,4]

PATHOPHYSIOLOGY OF UNSTABLE ANGINA:

The majority of patients with unstable angina (UA) have significant obstructive atherosclerosis. Episodes of ischemia can be evoked by an increase in myocardial oxygen demand (e.g., precipitated by tachycardia or hypotension) and/or by a reduction in supply (e.g., due to reduction in coronary diameter by platelet-rich thrombi or vasospasm).[5]

A sequence of events can be documented in UA in which there is first; a reduction in coronary sinus oxygen saturation (signifying a reduction in coronary blood flow), then ST segment depression, followed by chest discomfort.

A patient might have both a small increase in myocardial oxygen demand, in conjunction with a reduction in coronary blood flow, leading to the episode of ischemia.[6]

The factors that may lead to a new episode of ischemia are:

(1)INFLAMMATION AND/OR INFECTION: Inflammation appears to be a cause and not just a consequence of acute coronary syndromes. On a cellular level, leukocytes are activated in unstable angina, both in the systemic circulation and inside the culprit lesion.

Macrophages are capable of degrading extracellular matrix by phagocytosis or by secreting proteolytic enzymes, such as plasminogen activators and matrix metalloproteinases (MMPs)--collagenases (MMP-1), gelatinases (MMP-2 and MMP-9), stromelysins (MMP-3), and

matrilysin (MMP-7)--which may digest the matrix component of the fibrous cap, leading to thinning and predisposing it to disruption.

The ability of MMPs to induce matrix degradation is tightly regulated in part by co-secretion of tissue inhibitors of MMPs that neutralize the effects of MMPs as well as their secretion in a zymogen precursor form that requires extracellular activation. This activation of pro-MMPs can be induced by plasmin (generated by macrophages), tryptase, chymase (secreted by activated mast cells), oxidant stress, and exposure to oxidized LDL. Thus, the milieu in the atherosclerotic plaque is conducive to activation of pro-MMPs, thereby facilitating net matrix degradation.[7]

Besides macrophages, a wide variety of cells may produce MMPs, stimulate their production (T lymphocytes), or secrete proteolytic enzymes (mast cells) that activate MMPs once they are secreted.

In plaque disruption, the fibrous cap of a plaque tears, exposing the highly thrombogenic lipid-rich core to blood in the lumen of the artery. The mechanical strength of the plaque cap is therefore a vital component of plaque stability and depends on thickness, collagen content, and amount of other tissue proteins. A decline in smooth muscle cell density inevitably leads to a decline in collagen synthesis and thinning of the cap, making it more susceptible to rupture.[8]

Chronic infection has been found to be significantly associated with the development of atherosclerosis and the clinical complications of unstable angina, myocardial infarction, and stroke.

Potential mechanisms whereby chronic infections may play a role in atherogenesis are not well understood. In the case of Chlamydia pneumoniae infection, the effect may result from direct vessel wall colonization, which may damage the vessel directly or indirectly by initiating immunologic responses. In other cases, the effect may simply be that of enhancing the preexisting chronic inflammatory response of the body to standard risk factors, such as hyperlipidemia. Even though the infectious agent may not directly infect the vessel wall, it may perform its critical role from afar.[9]

One possible stimulator of MMP production in macrophages is chlamydial heat shock protein 60 (HSP60), which also was found to induce tumor necrosis factor synthesis in vitro. Furthermore, chlamydial HSP60 was frequently found to co-localize with human HSP60 in macrophages from human atherosclerotic lesions in carotid arteries, whereas neither HSP was found in non atherosclerotic tissue.[10]

Chronic infection might also influence preexisting plaque by enhancing T cell activation or other inflammatory responses that may participate in the destabilization of the intimal cap.

So chronic infection may play a role in the initiation, progression, or destabilization of atherosclerotic plaques.

The infectious agents with the most evidence to support a causative role in atherosclerosis include Chlamydia pneumoniae and cytomegalovirus. Evidence is mounting for a variety of other potential