Correlation between Brain Type Natriuretic Peptide Level and Severity of Coronary Artery Disease in Patients with Non-ST Elevation Acute Coronary Syndrome and Normal Left Ventricular Function

Thesis
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بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ

﴿وَعَلَّمَكَ مَا لَمْ تَكُنْ تَعْلَمُ وَكَانَ فَضْلُ اللَّهِ عَلَيْكَ عَظِيمًا﴾

صدق الله العظيم

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List of Abbreviations

Abb.	Full term
ACE	Angiotensin converting enzyme
ACS	Acute coronary syndrome
ARB	angiotensin-receptor blocker
BNP	Brain natriuretic peptide
BP	Blood pressure
CABG	Coronary bypass graft
CAD	coronary artery disease
CCB	Calcium Channel Blocker
CCS	Canadian Cardiovascular Society
CHF	Congestive heart failure
CK	Creatine kinase
CK-MB	Creatine kinase isoenzyme MB
CMR	Cardiac magnetic resonance
COPD	Chronic obstructive pulmonary disease
CPG	Committee for Practice Guidelines
CrCl	creatinine clearance
CRP	C-reactive protein
CRT	Cardiac resynchronization therapy
CT	Computed tomography
CTFC	Corrected TIMI frame count
DAPT	Dual antiplatelet therapy
DM	Diabetes Mellitus
ECG	electrocardiogram
eGFR	estimated glomerular filtration rate
GP IIb/IIIa	Glycoprotein IIb/ IIIa
GRACE	Global Registry of Acute Coronary Events
GS	Gensini Score
HF	Heart failure
hsCRP	High sensitivity C-reactive protein
LAD	Left anterior decending artery
LBBB	Left bundle branch block
LCX	Left circumflex artery(LCX)
LDL-C	Low density lipoprotein cholesterol

List of Abbreviations **cont...**

Abb.	Full term
LMCA	Left main coronary artery
LMWH	Low Molecular Weight Heparin
LV	Left ventricle
LVEDD	Left ventricular end diastolic diameter
LVEF	Left ventricle ejection fraction
LVESD	Left ventricular end systolic diameter
MACE	Major adverse cardiac events
MI	Myocardial infarction
MRI	Magnetic resonance imaging
MVD	Multivessel disease
MVO 2	Myocardial oxygen consumption
NSTE-ACS	Non ST elevation acute coronary syndrome
NSTEMI	Non ST elevation myocardial infarction
NT-proBNP:	N terminal prohormone brain natriuretic peptide
PCI	Percutaneous coronary intervention
RCA	Right coronary artery
STEMI	ST-elevation myocardial infarction
TIMI	Thrombolysis in Myocardial Infarction
UA	Unstable Angina
UFH	Unfractionated heparin

INTRODUCTION

Acute coronary syndrome (ACS) has evolved as a useful operational term that refers to a spectrum of conditions compatible with acute myocardial ischemia and/or infarction that are usually due to an abrupt reduction in coronary blood flow. A key branch point is ST-segment elevation or new left bundle-branch block on the electrocardiogram (ECG), which is an indication for immediate coronary angiography to determine if there is an indication for reperfusion therapy to open a likely completely occluded coronary artery. Separate committee for practice guidelines (CPGs) have been developed for ST-elevation myocardial infarction (STEMI) ***(O'Gara et al., 2013).***

The absence of persistent ST-elevation is suggestive of Non ST elevation acute coronary syndrome (NSTE-ACS) except in patients with true posterior myocardial infarction MI. NSTE-ACS can be further subdivided on the basis of cardiac biomarkers of necrosis (eg, cardiac troponin,). If cardiac biomarkers are elevated and the clinical context is appropriate, the patient is considered to have Non ST elevation myocardial infarction (NSTEMI) ***(Newby et al., 2012)***; otherwise, the patient is deemed to have unstable angina (UA). ST depression, transient ST-elevation, and/or prominent T-wave inversions may be present but are not required for a diagnosis of NSTEMI. Abnormalities on the ECG and elevated troponins in isolation are insufficient to make the diagnosis of ACS but must be

interpreted in the appropriate clinical context. Thus, UA and NSTEMI are closely related conditions whose pathogenesis and clinical presentations are similar but vary in severity.

The conditions differ primarily by whether the ischemia is severe enough to cause myocardial damage leading to detectable quantities of myocardial injury biomarkers.

The term "possible ACS" is often assigned during initial evaluation if the ECG is unrevealing and troponin data are not yet available. UA can present without any objective data of myocardial ischemic injury (normal ECG and normal troponin), in which case the initial diagnosis depends solely on the patient's clinical history and the clinician's interpretation and judgment. However, with the increasing sensitivity of troponin assays, biomarker-negative ACS (ie, UA) is becoming rarer ***(Braunwald and Morrow, 2013).***

Aim of the Work

The aim of this work is to assess the relationship between the level of BNP and the severity of coronary artery disease as assessed by Gensini score in patients who have unstable angina and non ST elevation myocardial infarction with normal left ventricular systolic function.

Chapter One

NON ST ELEVATION ACUTE CORONARY SYNDROME

Pathophysiology

Factors involved in the pathophysiology of NSTE-ACS ***(Stone et al.,2011)*** include the following:

1) Supply-demand mismatch

The myocardial ischemia of unstable angina, like all tissue ischemia, results from excessive demand or inadequate supply of oxygen, glucose, and free fatty acids.

2) Plaque disruption

Accumulation of lipid-laden macrophages and smooth muscle cells, so-called foam cells, occurs within atherosclerotic plaques. The oxidized low-density lipoprotein cholesterol (LDL-C) in foam cells is cytotoxic, procoagulant, and chemotactic. As the atherosclerotic plaque grows, production of macrophage proteases and neutrophil elastases within the plaque can cause thinning of the fibromuscular cap that covers the lipid core.

Increasing plaque instability, coupled with blood-flow shear and circumferential wall stress, leads to plaque fissuring or rupture especially at the junction of the cap and the vessel wall.

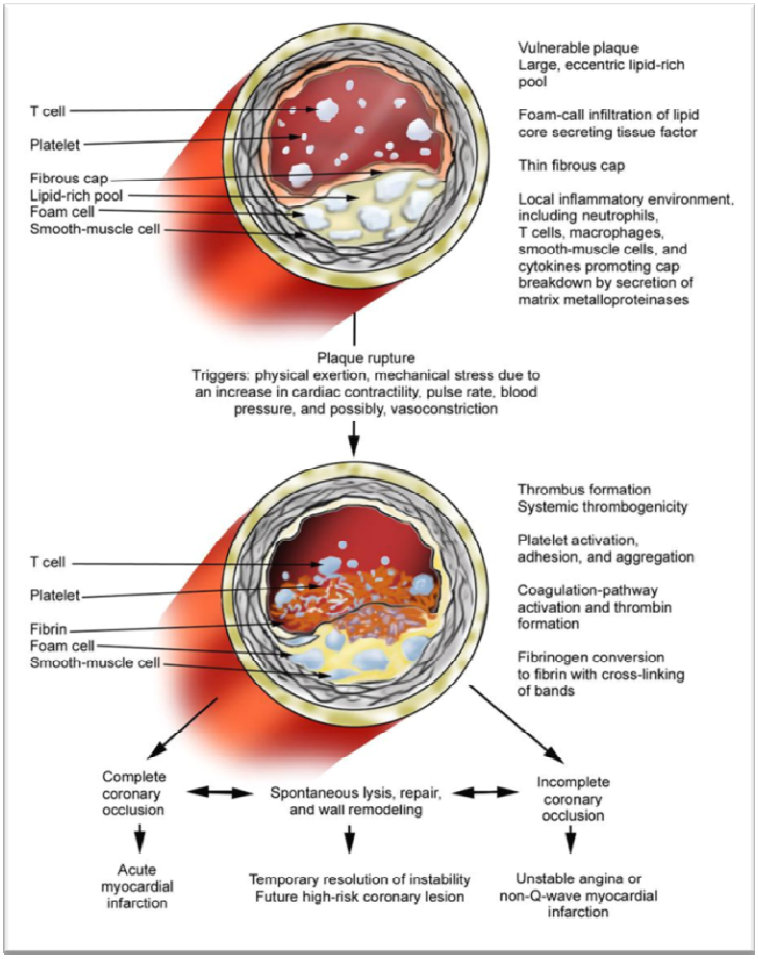

Figure (1): Atherosclerotic plaque in ACS.

3) Vasoconstriction and thrombosis

Most patients with ACS have recurrent transient reduction in coronary blood supply because of vasoconstriction and thrombus formation at the site of atherosclerotic plaque rupture. These events occur as consequences of episodic platelet aggregation and complex interactions among the vascular wall, leukocytes, platelets, and atherogenic lipoproteins.

Exposure of subendothelial components provokes platelet adhesion and activation. Platelets then aggregate in response to exposed vessel wall collagen or local aggregates (eg, thromboxane and adenosine diphosphate). Platelets also release substances that promote vasoconstriction and production of thrombin.

ACS may involve a clot in flux (ie, forming and enlarging, chipping off and embolizing). Over time, this dynamic clot formation or lysis, in conjunction with coronary vasoreactivity and resistance in the microvascular bed, causes intermittent and alternating (or cyclical) occlusion and flow.

- ***Clinical presentation***

The clinical presentation of NSTE-ACS encompasses a wide variety of symptoms. Traditionally, several clinical presentations have been distinguished:

- ***Prolonged (>20 min) anginal pain at rest***
- New onset (*de novo*) angina: Class II or III of the Classification of Canadian Cardiovascular Society (CCS) ***(Campeau, 1976).***
- Recent destabilization of previously stable angina with at least Canadian Cardiovascular Society Class III angina characteristics (crescendo angina).
- Post-MI angina