Assessment of Microalbuminuria as a Cardiovascular Risk in Patients with Metabolic Syndrome

Thesis

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List of Abbreviations

ACE.....**A**ngiotensin converting enzyme
ACR.....**A**lbumin creatinine ratio
ACS.....**A**cute coronary syndrome
AER.....**A**lbumin excretion ratio
ALT.....**A**lanine transminase
AMI.....**A**cute myocardial infarction
AST.....**A**spartate transminase
ATPIII.....**A**dult treatment panel III
BMI.....**B**ody mass index
BP.....**B**lood pressure
CA.....**C**oronary angiography
CAA.....**C**arotid artery atherosclerosis
CABG.....**C**oronary artery bypass graft
CAD.....**C**oronary artery disease
CHD.....**C**oronary heart disease
CLA.....**C**onjugated linoleic acid
CMV.....**C**ytomegalovirus
CP.....**C**hlamydia pneumonia
CRP.....**C**-reactive protein
CVD.....**C**ardiovascular disease
CVRF.....**C**ardiovascular risk factors
DBP.....**D**iastolic blood pressure
DM.....**D**iabetes mellitus
ECG.....**E**lectrocardiogram
EDNo.....**E**ndothelium derived nitric oxide

EH.....**E**ssential hypertension

ELISA.....**E**nzyme linked immunosorbant assay

ESR .....**E**rythrocyte sedimentation rate

ESRD.....**E**nd stage renal disease

FFA.....**F**ree fatty acids

GFR.....**G**lomerular filtration rate

HAV.....**H**epatitis a virus

HDL.....**H**igh density lipoprotein

HP.....**H**aemophilus pneumonia

HPA.....**H**ypothalamic- pituitary- adrenal axis

HR.....**H**eart rate

HSV.....**H**erpes simplex virus

IDF.....**I**nternational diabetic federation

IHD.....**I**schemic heart disease

IL-6.....**I**nterleukin-6

IMCL.....**I**ntra myocellular fat

IR.....**I**nsulin resistance

IRI.....**I**nsulin resistance index

IRS.....**I**nsulin resistance syndrome

IRS-1.....**I**nsulin receptor substrate-1

IS.....**I**nsulin sensitivity

LCACOA.....**L**ong chain aceyl-coA

LCPUF AS....**L**ong chain polyunsaturated fatty acids

LDL.....**L**ow density lipoprotein

MAA.....**M**acroalbuminuria

METS.....**M**etabolic syndrome

MI.....**M**yocardial infarction

MIA.....**M**icroalbuminuria

NA .....**N**ormoalbuminuria

NCEP.....**N**ational cholesterol education program

NIDDM.....**N**on insulin diabetes mellitus

NO.....**N**itric oxide

NSTEMI.....**N**on st elevation myocardial infarction

PAD.....**P**eripheral artery disease

PPAR-Y.....**P**eroxisome proliferator-activated receptor y

PVR.....**P**eripheral vascular resistance

RAS.....**R**enin-angiotensin system

SBP.....**S**ystolic blood pressure

SNS.....**S**ympathetic nervous system

STEMI .....**S**t elevation myocardial infarction

TC.....**T**otal cholesterol

TNF.....**T**umor necrosis factor

TNF-A.....**T**umor necrosis factor -a

T-PA-AG ....**T**issue type-plasminogen activator antigen

U.S .....**U**nited state

UAE .....**U**rinary albumin excretion

UAER .....**U**rinary albumin excretion rate

VLDL .....**V**ery low density lipoprotein

VWF .....**v**on Willebrand factor

WHO .....**W**orld health organization

Contents

List Of Tables

List Of Figures

List Of Figures *(Cont..)*

INTRODUCTION

The prevalence of metabolic syndrome is very high in coronary artery disease patients. The metabolic syndrome confers a higher risk of long-term major adverse cardiac and cerebral events *(Hu et al., 2006).*

WHO clinical criteria for metabolic syndrome insulin resistance identified by one of following:

- Type 2 diabetes
- Impaired fasting glucose
- Impaired glucose tolerance

Plus any 2 of the following:

- Antihypertensive medication and/or high blood pressure 140mmHg systolic and/or 90mmHg diastolic.
- Plasma triglycerides >150mg/dL.
- High density lipoproteins (HDL) <35mg/dL in men and <39mg/dL in women.
- Waist: hip ratio >0.9 in men and >0.85 in women albumin: creatinine ratio 30mg/g.

(Alberti et al., 1998; WHO, 2003)

The national cholesterol education program (NCEP) adult treatment panel III (ATP III) guidelines recommend that patient with at least 3 of the following clinical variables be designated as having metabolic syndrome: abdominal obesity as reflected in increased waist circumference; a law high-density lipoprotein cholesterol (HDI- C) level<35mg/dL in men and <39mg/dL in women, an elevated triglyceride level >150mg/dL, elevated blood pressure >140/90 or treatment with antihypertensive medication; and/or elevated fasting plasma glucose >100mg/dL or treatment with antidiabetic medication. Unless patients with metabolic syndrome change their lifestyle, existing cardiovascular and metabolic risk factors will be worsen or new risk factors will develop. This helps explain why these patients are at increased risk for type 2 diabetes mellitus (DM) and coronary heart disease (CHD) *(Stone et al., 2006).*

Combinations of risk factors of metabolic syndrome were frequently than coincidental phenomenon in the subjects from the general population. These finding suggest that these risk factors do cluster and obesity and insulin resistance were suggested to be linked with metabolic syndrome more than hypertension or high triglyceride *(Morpito et al., 2006).*

The metabolic syndrome is common among subject with diabetes and is a very common risk factor of macrovascular complications however; its contribution to the microvascular complication has not been assessed *(Nawaf et al., 2006).*

Micoralbuminuria a urinary albumin excretion of greater than 30mg/gm creatinine. Microalbuminuria is an important predictor of cardiovascular events and forms one of the component of the insulin resistance/metabolic syndrome, which confers a particularly high risk of cardiovascular death *(Erdmann et al., 2006).*

AIM OF THE WORK

The aim of the study is to assess the correlation between microalbuminuria and extent and severity of coronary artery disease by coronary angiography among patients with metabolic syndrome.

ATHEROSCLEROSIS

Risk factors for atherosclerosis:

1) Hypertension:

Basic researches had suggested that hypertension plays an important role in the pathogenesis of atherosclerosis. Indeed, elevated systolic blood pressure (SBP) and diastolic blood pressure (DBP) have consistently been associated with increased risk of atherosclerotic cardiovascular disease (CVD) in prospective population studies *(Kannel et al., 1996).* Additional evidence for the role of hypertension as a victor of CVD is derived from randomized trials, in which the treatment of Elevated blood pressure (BP) with antihypertensive drugs has reduced CVD *(Hansson et al., 1998).* Even mildly elevated SBP and DBP have been related to increased CVD in prospective population studies. Support for this finding comes from randomized trials that have shown a large cardiovascular benefit from the treatment complicated hypertension *(Jean-Charles et al., 2004).*

Hypertension could cause atherosclerosis through a number of possible mechanisms: impaired endothelium-dpendent arterial relaxation, enhanced monocytes and lymphocytes adherence to the

endothelium and migration into the intima, enhanced macrophages accumulation in the intima, and cytokine expression, stimulated smooth-muscle cells proliferation, raised plaque cellularity, increased susceptibility to intimal tears due to raised medial collagen synthesis and reduced arterial wall elasticity, increased cellular oxidative stress and oxygen-free radical production by the arterial wall and raised hypoxia caused by increased diffusion distances due to intimal thickening *(Jean-Charles et al., 2004).*

Hypertension also increases the wall shear stress and barotrauma to the arterial intima. increased flow velocity and wall shear stress are considered to be the important factor that causes hypertension-induced intima-media hypertrophy and thickness. hypertension is also associated with insulin resistance and considered a life station of metabolic syndrome *(Saito et al., 2002).*

The thickening of carotid intima is initiated when hypertension is borderline, but is not increase to cause significant carotid stenosis (after adjusting for other factors). This finding indicates that borderline hypertension (A transition to full-blown hypertension) may increase the risk of atherosclerosis, implying the increase in intima is an earlier preclinical atherosclerotic change. As