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List of Abbreviations

ACE inhibitors	: Angiotensin-Converting Enzyme Inhibitors
ANP	: Atrial natriuretic peptide
BAB	: Beta adrenergic blockers
BMI	: Body Mass Index
BNB	: brain natriuretic peptide
CAD	: Cardiovascular disease
CPT-1	: carnitine palmityltransferase- 1
CRP	: C-Reactive protein
CRT	: Cardiac Resynchronization Therapy
EGIR	: European Group for the Study of Insulin Resistance
ER	: Endoplasmic reticulum
EF	: Ejection Fraction
FFAs	: Free Fatty Acids
GDM	: Gestational diabetes mellitus
HDL	: High Density Lipoprotein
HF	: Heart Failure
Hs-CRP	: Highly sensitive C-reactive protein
HSL	: Hormone-sensitive lipase
IABP	: Intraaortic Balloon Counterpulsation
ICD	: Implantable Cardioverter Defibrillator
IDCM	: Idiopathic dilated cardiomyopathy
IDF	: International Diabetes Federation
IFG	: Impaired fasting glucose
IGT	: Impaired glucose tolerance
IGF-1	: Insulin-like growth factor 1

IRS-1	: Insulin receptor substrate
Mets	: Metabolic syndrome
MHC	: Myosin heavy chain
NAFLD	: Nonalcoholic fatty liver disease
NASH	: Nonalcoholic steatohepatitis
NCEP-ATPIII	: National Cholesterol Education Program
NE	: Norepinephrine
NHANES	: National Health and Nutrition Survey
OSA	: Obstructive sleep apnea
OXPHOS	: Oxidative phosphorylation
PAL-1	: Plasminogen activator inhibitor-1
PARP	: Poly ADP-ribose polymerase- 1
PCOS	: Polycystic ovarian syndrome
PDE	: Phosphodiesterase inhibitors
PGI₂	: Prostaglandins I ₂
RAAS	: Renin angiotensin–aldosterone system
SERCA-2	: Sarcoplasmic reticular Ca ²⁺ ATPase
SES	: Socioeconomic status
SNS	: Sympathetic nervous systems
SOLVD	: Studies of left ventricular dysfunction
T2D	: Type 2 Diabetes Mellitus
TNF	: Tumor necrosis factor
VADs	: Ventricular Assist Devices
VIP	: Vasoactive intestinal peptide
VLDL	: Very low-density lipoprotein
WC	: Waist Circumference

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Association Between Metabolic Syndrome and Heart Failure

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العلاقة بين المتلازمة الأيضية و فشل القلب

رسالة

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مقدمة من

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

لسبب أنك لا تعلم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدقة الله العظيم

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Introduction

The "metabolic syndrome" (MetS) is a clustering of components that reflect overnutrition, sedentary lifestyles, and resultant excess adiposity. The MetS includes the clustering of abdominal obesity, insulin resistance, dyslipidemia, and elevated blood pressure and is associated with other comorbidities including the prothrombotic state, proinflammatory state, nonalcoholic fatty liver disease, and reproductive disorders. Because the MetS is a cluster of different conditions, and not a single disease, the development of multiple concurrent definitions has resulted (**Alberti et al., 2006**).

The prevalence of the MetS is increasing to epidemic proportions not only in the United States and the remainder of the urbanized world but also in developing nations. Most studies show that the MetS is associated with an approximate doubling of cardiovascular disease risk and a 5-fold increased risk for incident type 2 diabetes mellitus (**Alberti et al., 2006**).

Although it is unclear whether there is a unifying pathophysiological mechanism resulting in the MetS, abdominal adiposity and insulin resistance appear to be central to the MetS and its individual components. Lifestyle modification and weight loss should, therefore, be at the core of treating or

preventing the MetS and its components. In addition, there is a general consensus that other cardiac risk factors should be aggressively managed in individuals with the MetS (**Alberti et al., 2006**).

Aim of the Work

To identify the association between metabolic syndrome components and heart failure discussing the different therapeutic approaches of both of them.

Metabolic Syndrome

Definitions:

A. Nomenclature of the metabolic syndrome:

Although the term MetS has become widely used since its inception in 2001 by the National Cholesterol Education, the concept of "clustering" metabolic disorders and cardiovascular disease (CVD) risk factors has been discussed in the scientific literature for many decades. In fact, recent reviews have noted that independent scientists published reports of the association between diabetes mellitus and hypertension as early as the 1920s, when Kylin documented a connection between hypertension, hyperglycemia, and gout. While the primer for understanding visceral adiposity did not occur until nearly 30 yr later, by the early 1990s visceral obesity was fully appreciated as a component of the insulin resistance syndrome (**National cholesterol education, 2002**).

In 1980, the seminal work of Margair et al., Brink focused on the relationship between obesity, hypertriglyceridemia, and hypertension. It was not until 1988 when Reaven, in his landmark Banting Lecture, coined the term "Syndrome X" to describe the proposed interrelationships between resistance to insulin-stimulated glucose uptake, hypertension, type 2 Diabetes mellitus (T2D), and

Cardiovascular disease (CVD). During the ensuing 10 yr, Syndrome X and other terms were used to describe the clustering of cardiovascular and metabolic risk factors, including the "insulin resistance syndrome" (**Dana Dabelea et al., 2008**).

B. Definitions:

The first formal definition of the MetS was put forth in 1998 by the World Health Organization (WHO). This definition focused primarily on the presence of insulin resistance, identified by hyperinsulinemia, impaired glucose tolerance (IGT), or the diagnosis of type 2 diabetes, which had to be present to make the diagnosis. In addition, two of the following also had to be present: dyslipidemia (reduced HDL-C and increased triglycerides), hypertension, and microalbuminuria (Table 1) (**Rajesh Tota-Maharaj et al., 2010**).

Table (1): WHO definition of the metabolic syndrome.

Criteria For The Diagnosis

Insulin resistance, plus any two of the following parameters:

- Hypertension $\geq 140/90$ mmHg, or taking medication of previously diagnosed hypertension.
- Plasma triglycerides ≥ 150 mg/dL, low HDL, or both:
 - Men < 35 mg/dL
 - Women < 39 mg/dL
- BMI > 30 kg/m², waist-hip ratio (WHR), or both :
 - Men > 0.9 WHR
 - Women > 0.85 WHR
- Microalbuminuria.

(Rajesh Tota-Maharaj et al., 2010)

The European Group for the Study of Insulin Resistance (EGIR) published a separate set of criteria shortly thereafter. The basic premise of the EGIR definition was that the MetS "is a syndrome of mild anomalies which, in combination, increase cardiovascular risk." This definition, although similar to the WHO definition, did not include microalbuminuria (Table 2). The EGIR emphasized that the presence of microalbuminuria was not a requirement for one to have the MetS (**Dana Dabelea et al., 2008**).

Table (2): EGIR definition of the metabolic syndrome.

Criteria For The Diagnosis

Top 25% of the fasting insulin values among nondiabetic individuals and two of the following:

- WC: ≥ 94 cm for men, ≥ 80 cm for women
- Triglycerides ≥ 2.0 mmol/liter and HDL-C < 1.0 mg/dl
- BP $\geq 140/90$ mm Hg or antihypertensive medication
- Fasting glucose ≥ 6.1 mmol/liter

(Rajesh Tota-Maharaj et al., 2010)

In 2002, the National Cholesterol Education Program (NCEP:ATPIII) published a new set of criteria based on common clinical measurements: WC, blood lipids, blood pressure, and fasting glucose. The NCEP:ATPIII definition differed from both the WHO and EGIR definitions in that the