

EDITORIAL

Metabolic Syndrome: Search for Harmonized (Unified) Diagnostic Criteria

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Metabolic syndrome (MetS) is not a single disease but a cluster of different metabolic abnormalities like obesity, hypertension, hypertriglyceridemia, low HDL-c, insulin resistance, diabetes mellitus etc. The world wide prevalence of metabolic syndrome in adult population is on rise. It is a major public health challenge globally due to rapid urbanization, sedentary lifestyle and surplus energy intake. MetS has been linked to a two-fold increased risk of cardiovascular disease (CVD), five-fold increased risk of type 2 diabetes mellitus (T2DM), two to four-fold increased risk of stroke, three to four-fold of increased risk of myocardial infarction and two-fold increased risk of dying from such events over the following five to ten years. The worldwide prevalence of MetS in adults has been estimated to be 20-25%. It is increasingly prevalent in both developed and developing nations.

Reaven was the first to put forward the concept of 'Syndrome X', (which he later renamed as MetS), hypothesizing that it was a central feature in the development of coronary artery disease (CAD) and type 2 diabetes mellitus (T2DM), mainly through target tissue resistance to insulin action. Since then, many international organizations and expert groups, such as the World Health Organization (WHO), the European Group for the study of Insulin Resistance (EGIR), the National Cholesterol Education Program: Adult Treatment Panel III (NCEP: ATP III), the American Association of Clinical Endocrinology (AACE) and the International Diabetes Federation

(IDF), attempted to define MetS addressing different parameters. The first attempt was made in 1998 by the WHO, which proposed that MetS may be defined by the presence of insulin resistance (IR) or its surrogates e.g., impaired glucose tolerance (IGT) or type 2 diabetes mellitus (T2DM), as essential components of the syndrome, along with at least two of the following parameters: hypertension, hypertriglyceridemia and/or low HDL-cholesterol, obesity & microalbuminuria. Shortly thereafter, the EGIR excluded microalbuminuria as an integral component of the metabolic syndrome, while it added hyperinsulinemia to be present.

In 2001, the NCEP ATP III published a new set of criteria that included waist circumference, blood lipids, blood pressure and fasting blood glucose. The NCEP ATP III definition differed from both the WHO and EGIR definition in that insulin resistance was not considered as a necessary diagnostic component by NCEP: ATP III. In 2005, the International Diabetes Federation (IDF) published newer criteria in this regard. The IDF introduced abdominal obesity as a prerequisite of the diagnosis of MetS, with particular emphasis on waist circumference measurement. Although each definition possesses many common features but clear heterogeneity exist among them. Currently, the two most widely used definitions are those of the NCEP: ATP III and IDF focusing specifically on waist circumference, which is a surrogate measure of central obesity. In contrast, the AACE, WHO and the EGIR definitions are all largely focused on insulin resistance.

It is clear that, an early detection of metabolic syndrome is the corner stone to prevent the subsequent development of T2DM, CVD, MI, stroke etc among these individuals. Due to heterogeneity among different diagnostic criteria of MetS, there is

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fair chance of false positive and false negative diagnosis if we like to decide depending on one definite diagnostic criteria. Therefore, we are in crying need to explore for an unified diagnostic criteria of MetS.

WHO definition of MetS¹

WHO defined MetS as the coexistence of impaired glucose tolerance (IGT) or diabetes mellitus together with insulin resistance (IR) and presence of at least two of the following components:

- Raised blood pressure, i.e., blood pressure (BP) $\geq 140/90$ mmHg
- Raised plasma triacylglycerol (≥ 150 mg/dl) and/or low HDL-C (< 35 mg/dl in men and < 39 mg/dl in women)
- Central obesity, i.e., waist/hip ratio (WHR) ≥ 0.9 in men and ≥ 0.85 in women and/or body mass index (BMI) ≥ 30 kg/m² irrespective of gender
- Microalbuminuria, i.e., urinary albumin excretion rate ≥ 20 μ gm/minute or albumin/creatinine ratio (ACR) ≥ 30 μ gm/mg.

American Association of Clinical Endocrinologists (AACE) definition of MetS²

AACE placed emphasis on clinical judgement more instead of providing as specific set of diagnostic criteria. The following diverse components were proposed by AACE:

- Fasting plasma glucose (FPG) ≥ 6.1 mmol/L
- Blood glucose 2 hrs after breakfast ≥ 7.8 (but not T2DM)
- BMI ≥ 25 kg/m²
- Raised blood pressure, i.e., $\geq 130/85$ mm of Hg
- Raised plasma triacylglycerol ≥ 150 mg/dl
- Low HDL-C (< 40 mg/dl in men and < 50 mg/dl in women)
- Abnormal uric acid metabolism
- Hemodynamic changes etc.

European Group for the Study of Insulin Resistance (EGIR) definition of MetS³

As per EGIR definition, diagnosis of MetS requires the presence of elevated insulin levels in blood coupled with at least two other characteristics from the following list:

- Abdominal obesity: waist circumference (WC) ≥ 94 cm in men and ≥ 80 cm in women
- Hypertension: blood pressure $\geq 140/90$ mmHg or on antihypertensive treatment

- Elevated triacylglycerol (≥ 150 mg/dl) and/or reduced HDL-C (< 39 mg/dl for both men and women)
- Elevated plasma glucose: Impaired fasting glucose (IFG) or impaired glucose tolerance (IGT), but no diabetes.

Modified National Cholesterol Education Program: Adult Treatment Panel III (Modified NCEP-ATP III) definition of MetS⁴

According to this definition, an individual will be considered to have MetS if they meet three or more of the following criteria:

- Elevated waist circumference; for Asian ≥ 102 cm (≥ 35 inches) in men or ≥ 88 cm (31 inches) in women
- Elevated triacylglycerol: ≥ 150 mg/dl or on drug therapy for elevated triacylglycerol
- Reduced HDL-C: < 40 mg/dl in men, < 50 mg/dl in women or on drug therapy for reduced HDL-C
- High blood pressure: systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mm of Hg or on antihypertensive drug treatment
- Elevated fasting plasma glucose: ≥ 110 mg/dl (6.1 mmol/L) or on drug therapy for elevated plasma glucose.

International Diabetes Federation (IDF) definition of MetS⁵

The IDF has established a precise definition for MetS, incorporating specific waist circumference (WC) cut offs tailored to different races and genders. This definition includes central obesity (as determined by waist circumference cutoffs for different races and genders; for Asian males ≥ 90 cm and females ≥ 80 cm) and any two of the following four characteristics:

- Raised triacylglycerol: ≥ 150 mg/dl or on drug for raised triacylglycerol
- Reduced HDL-c: < 40 mg/dl in males and < 50 mg/dl in females or on drug for low HDL-c
- Raised blood pressure: systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg or on treatment of hypertension.
- Raised fasting plasma glucose: ≥ 5.6 mmol/L.

Harmonized (Unified) definition of MetS⁶

IDF, AHA (American heart association), NHLBI (National heart, lung & blood institute), World Heart Federation, International Atherosclerosis Society and International Association for the Study of Obesity released collaborative interim declaration in an attempt to unify diagnostic criteria of MetS. They proposed that one has to meet three of the following five criteria for diagnosis of MetS:

1. Geographic and ethnic specific waist circumference (WC) in cm

Population / ethnicity	Male	Female
United States	≥102	≥88
Canada	≥102	≥88
Europoid	≥ 94	≥80
European Cardiovascular Societies	≥102	≥88
South Asian	≥90	≥80
Chinese	≥90	≥80
China Cooperative Task Force	≥85	≥80
Japanese	≥85	≥90
Ethnic South and Central Americans	≥90	≥80
Eastern Mediterranean & Middle East	≥94	≥80
Sub-Saharan African	≥94	≥80

2. HDL-C: Male <40 mg/dl and Female < 50 mg/dl
3. Triacylglycerol: ≥150 mg/L or under treatment for high triacylglycerol
4. Fasting plasma glucose: ≥100 mg/dl (5.6 mmol/L) or under treatment for high fasting plasma glucose

5. Hypertension: systolic blood pressure ≥130mmHg or diastolic blood pressure ≥85mmHg or under treatment of hypertension

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