Editor's Note

The Metabolic Syndrome: Is it Really a Syndrome?

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In 2006, the “metabolic syndrome” has become a rather fashionable entity that is being discussed many times in our scientific journals. My question is, “Is it really a syndrome?” The definitions of a syndrome are as follows: (i) a group of signs and symptoms considered together as characteristic of a particular disease; (ii)

the aggregation of signs

and symptoms associated with any morbid process and together constituting the picture of the disease.

I have always thought of a syndrome as a pathological finding associated with clinical signs. As a medical student, the first syndrome that I ever learned about was the Foster–Kennedy syndrome. The Foster–Kennedy syndrome is due to a frontal lobe tumor, usually an olfactory groove meningioma, which compresses the optic nerve in one eye and results in optic atrophy in that eye and papilledema in the other eye because of increased intracranial pressure.

The so-called metabolic syndrome is not a tidy package in which specific pathology results in abnormal signs and symptoms. Rather, it is a clustering of clinical and laboratory abnormalities associated with a high risk for developing diabetes and/or cardiovascular disease. In fact, there is no uniform definition. At present, a metabolic syndrome is defined by three different sources [i.e., Adult Treatment Panel III, International Diabetes Federation (IDF), and World Health Organization (WHO)]. Their characterization of the “metabolic syndrome” is not exactly the same, although there is

TABLE 1 Differences and similarities of the three “metabolic syndrome” definitions by three different sources

Cardiometabolic risk factors	ATP III	WHO	IDF
Abdominal obesity (waist circumference)	(+)	(–)	(+)
Waist–hip ratio	(–)	(+)	(–)
BMI	(–)	(+)	(–)
Triglycerides	(+)	(+)	(+)**
↓ High-density lipoprotein cholesterol	(+)	(+)	(+)**
BP	(+)	(+)*	(+)*
Fasting glucose	(+)	(+)	(+)
Type 2 diabetes	(–)	(+)	(+)
Microalbuminuria	(–)	(+)	(–)
Uric acid	(–)	(–)	(–)
C-reactive protein	(–)	(–)	(–)

Abbreviations: * = or receiving anti-hypertensive, ** = or receiving treatment medication, ATP III = Adult Treatment Panel III, WHO = World Health Organization, IDF = International Diabetes Federation, BMI = body mass index, BP = blood pressure, “+” = included in the definition, “–” = not included in the definition.

some overall consistency. The differences and similarities are summarized in Table 1.

ATP III Definition

The definition of ATP III is abdominal obesity >40 in for men and >35 in for women, triglycerides >150 mg/dL, High-density lipoprotein cholesterol (HDL) <40 mg/dL in men and <50 mg/dL in women, blood pressure ≥ 130 over ≥ 85 mmHg and fasting glucose >110 mg/dL (the American Diabetes Association [ADA] has now changed this to ≥ 100 mg/dL.) The National Cholesterol Education Program (NCEP) (ATP III) definition of the “metabolic syndrome” states that three of the five factors must be present; i.e. increased waist circumference, hypertriglyceridemia, low HDL, hypertension, and fasting serum glucose >110 mg/dL.

International Diabetes Federation Definition

The diagnosis of “metabolic syndrome” based on the IDF criteria emphasizes central obesity. Central obesity is defined according to waist circumference, which is ethnic- and gender specific.

Central obesity plus any two of the following defines the “metabolic syndrome”:

- plasma triglycerides >150 mg/dL
- HDLC <40 mg/dL
- blood pressure $\geq$ 140/90 mmHg
- fasting glucose >100 mg/dL
- previously diagnosed type 2 diabetes.

World Health Organization Definition

The WHO emphasizes the central role of insulin resistance. Insulin resistance is defined as type 2 diabetes, or impaired fasting glucose, or a fasting glucose greater than 110 mg/dL. This is in addition to any two of the following:

- taking antihypertensive medication and/or blood pressure >140/90 mmHg
- plasma triglycerides >150 mg/dL
- HDLC <35 mg/dL for men or <39 mg/dL for women
- BMI >30 kg/m² and/or waist-hip ratio >0.9 (men); >0.85 (women)
- urinary albumin excretion rate $\geq$ 20 μ g/min or albumin-creatinine ratio $\geq$ 30 mg/g.

Abnormalities Associated with the “Metabolic Syndrome”

Many have reported other abnormalities associated with the “metabolic syndrome”, including the following:

- a nondipping pattern of 24 h blood pressure or salt-sensitive hypertension
- endothelial dysfunction
- increased plasminogen activator inhibitor
- increased platelet aggregation
- microalbuminuria
- $\uparrow$ uric acid
- $\uparrow$ C-reactive protein.

Metabolic Syndrome or Cardiometabolic Risk?

Since there are three major definitions of a “metabolic syndrome,” I think it may be more appropriate to

consider these laboratory and physical examination abnormalities as cardiometabolic risk factors rather than as syndromes. Cardiometabolic risk is a collection of abnormal body measurements and abnormal laboratory tests that may identify people at high risk for developing diabetes and cardiovascular disease.

I believe that obesity is the major global problem that results in this increased cardiometabolic risk. Obesity is a major contributor to insulin resistance, but there are other situations in which insulin resistance may be common, such as increased uric acid, family history of type 2 diabetes or coronary artery disease.

Microalbuminuria is also an important risk factor because it can be elevated in patients with glucose intolerance, and it is highest in patients with overt diabetes mellitus. The new enemy is our appetite. One in every four people on earth is too fat; 1.7 billion people should lose weight. Obese people now outweigh all the hungry people in the world.

What Should be Done to Manage Patients with Cardiometabolic Risk?

The majority of patients seen in cardiology practices have insulin resistance. Synergistic interaction of known cardiac risk factors associated with insulin resistance places patients at high risk for cardiovascular disease. Current guidelines recommend aggressive multifactorial treatment in patients with diabetes or prediabetes. The goal of therapy is to reduce the risk for diabetes, myocardial infarction, stroke, sudden cardiac death, and any other manifestation of coronary, peripheral arterial and kidney disease by reducing the collection of common risk factors that result in a high risk for cardiometabolic disease.

For managing these patients, a multidisciplinary consensus by the American Health Association, NHLBI, and the ADA include the following:

1. modifying lifestyles (weight loss, increasing physical activity, smoking cessation)
2. assessing risk with the Framingham Risk Score
3. reducing known risk factors (i.e., elevated lipids, elevated blood pressure, potential for thrombosis, abnormal glucose metabolism, and possibly uric acid and C-reactive protein).

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