Metabolic Syndrome: A Definition in Progress

We applaud the National Heart, Lung and Blood Institute and the American Heart Association in their efforts to define and outline the pathophysiology of the complex and still ill-defined metabolic syndrome.1 Although there is little doubt that obesity is closely linked to many components of the metabolic syndrome, we must also acknowledge that much of the data available on the metabolic syndrome are derived from (large) registries and post hoc analyses of clinical studies2,3 that are not specifically designed to address the relationship between obesity, measures of insulin resistance, and other associated features of the metabolic syndrome, and eventual cardiovascular outcome. These studies provide useful associations but do not establish the temporal relationship between obesity, insulin resistance, and other independent factors (such as serum lipid levels). In the absence of an established temporal relationship (cause preceding effect) and clinical trials documenting improved cardiovascular outcome with reduced insulin resistance, we fear that the Committee’s description of “3 aetiological categories,” which implies a 1-way causal relationship, may be presumptuous (at this point in time) and may conceal a more complex pathophysiology.

Finally, body mass index (BMI), though widely used, is not sensitive to adverse levels of obesity in all populations across different ethnic groups. Indeed, South Asians have higher upper body and visceral fat for a given BMI when compared with people of European descent.4 Hence, obesity should be defined in the context of specific ethnic population, which is reflected in the recent World Health Organisation recommendation of a lower BMI in South Asians (BMI over 23 kg/m² classed as overweight). The concept of “primary insulin resistance,” as proposed by the Committee, has not been clearly defined, detracts from the ethnic-specific anthropometric differences, and risks introducing further confusion.

Hoong Sern Lim, MRCP
Jeetesh V. Patel, PhD
Gregory Y.H. Lip, MD, FRCP
Haemostasis, Thrombosis, and Vascular Biology Unit
University Department of Medicine
City Hospital
Birmingham, UK
g.y.h.lip@bham.ac.uk

Response

In response to the letter of Lim, Patel, and Lip, allow me to respond for the writing group that produced the summary conference on definition of the metabolic syndrome sponsored by the National Heart, Lung and Blood Institute (NHLBI) and American Heart Association (AHA).1 We appreciate your interest in this conference and your willingness to comment in writing.

First, there is an enormous body of data of many types that document that obesity is accompanied by an increase in metabolic risk factors that predispose to cardiovascular disease.2 These risk factors include higher cholesterol and triglyceride, lower high-density lipoprotein (HDL), higher blood pressure, insulin resistance, and elevated glucose, including type 2 diabetes. Moreover, obesity is accompanied by several other emerging risk factors that underlie a prothrombotic state and a proinflammatory state.3 Finally, several prospective studies show that obesity is associated with increased risk for cardiovascular disease.3 The National Cholesterol Education Program (NCEP)4 views the metabolic syndrome as the constellation of cardiovascular risk factors that often accompany obesity.

The NCEP has not attempted to define the complex pathophysiological pathways that link obesity to the metabolic syndrome. A great deal of research is being carried out to better understand these pathways, but our knowledge is far from complete. Nevertheless, existing data strongly suggest that many persons are genetically predisposed to insulin resistance and other cardiovascular risk factors. When these people become obese, they are more likely to develop the metabolic syndrome in its more severe forms. Finally, the NCEP recommended using waist circumference as an indicator of obesity rather than body mass index.3 It noted that definitions of a high waist circumference vary in different populations.

Scott M. Grundy, MD, PhD
Center for Human Nutrition
University of Texas Southwestern Medical Center
Dallas, Tex

References


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Hoong Sern Lim, Jeetesh V. Patel and Gregory Y.H. Lip

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