

Preface

Metabolic Syndrome: Part II



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Guest Editor

The metabolic syndrome represents a constellation of risk factors for cardiovascular disease (CVD). These metabolic risk factors include atherogenic dyslipidemia and elevations of blood pressure, glucose, prothrombotic factors, and proinflammatory factors. Individuals who have the metabolic syndrome are at increased risk for type 2 diabetes as well as for CVD.

Current concepts of the metabolic syndrome represent the confluence of two merging streams of research. On the one hand, the metabolic syndrome is viewed by some investigators as representing largely the metabolic complications of obesity. Without doubt, obesity itself is a major underlying risk factor for both CVD and type 2 diabetes. It is accompanied by a variety of metabolic aberrations (risk factors) that more directly produce these two clinical outcomes. Another view holds that insulin resistance is the major underlying risk factor for the metabolic syndrome. There is no question that insulin resistance is a key risk factor for the development of type 2 diabetes. Furthermore, insulin resistance is commonly associated with the metabolic risk factors for CVD. A leader in the area of risk factors associated with insulin resistance is Dr. Gerald Reaven. He and many other investigators visualize a mechanistic (ie, causal) connection between insulin resistance and these metabolic risk factors; for this reason, the term *insulin resistance syndrome* often is used synonymously with *metabolic syndrome*.

A working group on the definition of diabetes organized by the World Health Organization (WHO) in 1998 proposed a “working definition” of the condition they called the *metabolic syndrome*. This definition was in fact a list of criteria for the clinical diagnosis of the condition. One requirement for

the diagnosis is the presence of evidence of insulin resistance. Other criteria were largely CVD risk factors of metabolic origin. In 2001, the United States National Cholesterol Education Program's Adult Treatment Panel III (ATP III) report proposed a somewhat different set of criteria for clinical diagnosis of the metabolic syndrome. The ATP III list of criteria had a similar structure as those proposed by the WHO working group; however, in contrast to the WHO criteria, direct evidence of insulin resistance was not required. More emphasis was placed on obesity (especially abdominal obesity) as a key component of the metabolic syndrome. The ATP III criteria further did not require special evaluation such as oral glucose tolerance testing. It used a simple measurement of fasting glucose to define impaired fasting glucose as one of the criteria. Importantly, both the WHO and ATP III did not exclude patients with type 2 diabetes from a diagnosis of metabolic syndrome provided they had other criteria. More recently, the American Association of Clinical Endocrinologists (AACE) has listed criteria for diagnosis of insulin resistance syndrome. The AACE placed emphasis on oral glucose testing to identify impaired glucose tolerance as one of the diagnostic criteria. It further excluded patients with type 2 diabetes from a diagnosis of insulin resistance syndrome. In spite of differences in approach to the metabolic syndrome diagnosis, there is much overlap among the different criteria; thus many of the same persons will be identified as having the syndrome regardless of the criteria employed.

All reports on the definition of the metabolic syndrome have mainly emphasized lifestyle therapies as first-line management. These therapies include weight reduction, increased physical activity, and changes in diet composition to optimize metabolic risk factors. The goals of lifestyle therapies are twofold: to modify CVD risk factors so as to reduce risk for CVD and to lower the risk for type 2 diabetes. One of the most important reasons for introducing the concept of the metabolic syndrome (or insulin resistance syndrome) into clinical practice is to heighten awareness of the increased risk associated with obesity and sedentary life habits in modern society. It has become apparent that the metabolic syndrome is a worldwide problem and has its origins largely in changes in patterns of food availability, eating habits, and physical activity. Treatment of the metabolic syndrome in clinical practice is therefore meant to amplify the public health approach to reducing the metabolic complications of obesity and physical inactivity.

In a portion of patients with the metabolic syndrome, drug therapies will be required to treat CVD risk factors of metabolic origins. On the list of medications are statins, fibrates, and nicotinic acid for atherogenic dyslipidemia, blood pressure-lowering drugs, hypoglycemic agents when patients have type 2 diabetes, and low-dose aspirin for a prothrombotic state. Use of these agents should be implemented according to current treatment guidelines. Very often drugs in combination will be necessary to control multiple risk factors. The presence of metabolic syndrome alone does not

justify drug therapies in most cases; but many patients with the metabolic syndrome will qualify for drug treatment according to existing guidelines.

An important but unresolved question is whether drugs that reduce insulin resistance should be employed in persons with the metabolic syndrome to reduce the risk for type 2 diabetes. There is growing evidence that such drugs—metformin and glitazones—will in fact reduce the risk for type 2 diabetes. What is not resolved is their cost effectiveness and long-term safety for this purpose. Clinical trials currently are underway to determine the effectiveness of these agents for reducing diabetes risk. These trials are further testing the possibility that these agents will reduce CVD independently of their effects on development of diabetes.

There has been a sharp upswing in interest in the metabolic syndrome on the part of the general public and medical community. This growing interest is driven by several factors: greater awareness of the dangers of obesity and its complications in the general public, advances in research on understanding the metabolic basis of the metabolic syndrome, therapeutic advances, and the presence of new guidelines that focus specifically on the metabolic syndrome. The reviews in the previous and current issue of the *Endocrinology and Metabolism Clinics of North America* provide an authoritative summary of the current status of the metabolic syndrome for clinical practice.

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