

Metabolic Syndrome: To Be or Not To Be?

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As pointed out in this issue's commentary by K.M. Venkat Narayan, MD, MPH, FRCP, FACP (p. 38), the association of several cardiovascular disease (CVD) risk factors—central obesity, hypertension, dyslipidemia, and abnormalities of glucose regulation—and their assumed interrelatedness with insulin resistance have led many experts in the field to link them into a distinct entity referred to as

“metabolic syndrome.” Much debate exists as to whether the identification of these risk factors as a “syndrome” is useful in terms of improved detection and earlier treatment aimed at reducing CVD risk.

As noted in the Narayan commentary, the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) have published a joint position statement recom-

mending against its identification as such and have raised important concerns about its therapeutic value. I refer you to our commentary, as well as the complete joint statement simultaneously published in *Diabetes Care*¹ and *Diabetologia*.²

There are many arguments, supported by numerous studies published in the literature, both for and against the usefulness of recognizing and treating patients as having a “metabolic syndrome” in

one's clinical practice. It is likely that many health care providers are confused by the controversy surrounding this issue. Should patients be identified as having a "syndrome," and if so, will it change the management aimed at reducing their CVD risk?

Let's look at the issues from both sides, from the perspective of scientific merit and the practical perspective of clinicians in the "real world." First, the ADA and EASD look at the syndrome definition with a rigorous scientific eye. They rightly point out that the criteria included in the definition are ambiguous, unclear, or incomplete and differ depending on which definition you use. Additionally, it is noted that the cut points used to define abnormal levels of the individual components are arbitrary and as such ignore the continuous relationship of each component with CVD risk. Further, it is unclear whether there is really a unifying pathophysiology underlying the existence of the syndrome (i.e. insulin resistance). Finally, while it is true that individual components of the metabolic syndrome are important predictors of CVD risk, it is not clear whether identifying them together as a "syndrome" adds to CVD prediction beyond the contribution of each component risk factor.

The American College of Endocrinology (ACE)/American Association of Clinical Endocrinologists (AACE) looks at the issue with more of a clinician's eye.³ It supports the idea of a "metabolic syndrome" or "insulin resistance syndrome" with an important clinical goal in mind: the early identi-

cation of individuals at risk for CVD and diabetes before these conditions develop. It suggests, too, that the presence of a syndrome will help to expand the concept of insulin resistance into other disease states (e.g., polycystic ovarian disease and nonalcoholic fatty liver disease). AACE feels that for practical purposes, the term "syndrome" is conceptually attractive and clinically useful. If examined from a patient's perspective, it may help to reinforce the appreciation of the coexistence of multiple risk factors for CVD and the need for treatment of all of these risk factors. To my mind, it also appropriately focuses right in on the number one environmental cause of insulin resistance—obesity—and the need to target it for treatment in its own right in order to reduce associated risk factors.

So while the metabolic syndrome may not be a disease unto itself, some may choose to utilize the concept in the care of patients who have its clinical components. I think we all agree it is still worth identifying patients who are at metabolic risk. Identification of a patient as having a "syndrome" may help the clinician to emphasize the global risk or make it seem more real to the patient. So to many clinicians or their patients, the concept may be clinically useful to help focus on treatment of multiple targets.

Scientifically, it is not a syndrome until we can agree on what criteria make its diagnosis, better clarify whether there is indeed a unifying underlying pathophysiology, and also devise thresholds that better reflect magnitude of risk based on hard scientific evidence.

Maybe when we have our "polypill"^{4,5} (i.e., the "one pill that treats all"), classifying it as a syndrome of interrelated risk factors will make more sense.

In the current state of drug availability, with no polypill at our disposal, treatment for the "syndrome" is no different from treatment for each of its individual components. But if the concept of a syndrome helps us to focus aggressively on identifying and treating all CVD risk factors present, how can it hurt?

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Note of disclosure: Dr. Marks has received honoraria or consulting fees from Sanofi-Aventis, which manufactures products for the treatment of diabetes and hypertension.

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