

The metabolic syndrome—is one global definition possible?

Reaven suggested in 1988 the existence of a cluster of metabolic abnormalities with insulin resistance as the central pathophysiological feature [1], and labelled it 'syndrome X'. The World Health Organization (WHO) and others have systematized this concept as 'the metabolic syndrome'. The presence of the syndrome is suggested to increase the risk of developing diabetes and cardiovascular disease (CVD). In his description of the syndrome Reaven considered the following abnormalities: resistance to insulin-stimulated glucose uptake, glucose intolerance, hyperinsulinaemia, increased triglycerides, decreased HDL-cholesterol, and hypertension. Since then several other metabolic abnormalities have been linked to insulin resistance including overall or abdominal obesity, microalbuminuria, hyperuricaemia, and plasminogen activator inhibitor 1. However, substantial uncertainties remain about the clinical definition of the syndrome and whether risk factor clusters collectively indicate a unifying underlying disorder or pathophysiological mechanism. Thus, there are two conceptually different approaches to the definition and understanding of the metabolic syndrome: (i) a biologically defined syndrome with insulin resistance as the unifying aetiology, and (ii) an epidemiologically defined syndrome where the metabolic syndrome is regarded as a cluster of metabolic risk factors that tend to occur in the same individual, providing a metabolic risk score primarily for CVD.

This issue of *Diabetic Medicine* reports two studies on the prevalence of the metabolic syndrome in rural and urban areas in South Korea according to the definition suggested by the WHO and the working definition published by The National Cholesterol Education Program (NCEP) Expert Panel [2,3]. In both studies the prevalence of the metabolic syndrome is as high as in western countries, and surprisingly the prevalence is only slightly higher in the urban compared with the rural area. A remarkably high prevalence is seen among women compared with men; however, among both men and women the syndrome occurs despite a low prevalence of overall and abdominal obesity.

Obesity is thought to be an important determinant of metabolic risk factors. The results of these studies suggest that genetic and/or behavioural factors associated with ethnicity may also contribute to these risk factors. It is well established that the association between obesity and metabolic risk factors varies across populations [4–6], and the fact that Asian populations are experiencing high levels of CVD at much lower levels of obesity than European populations has led to reassessment of the 'healthy range' of body mass index and waist circumference for Asian populations by the WHO [5]. However, the cut-off values for abdominal and overall obesity

included in the proposed definitions of the metabolic syndrome are based on studies of white Europeans, and its impact on metabolic factors should not uncritically be extrapolated to other ethnic groups. The study by Song *et al.* has taken this into consideration and included the revised criteria of abdominal obesity for Asian populations into the modified NCEP definition [3].

The study by Kim *et al.* compares the two proposed definitions of the metabolic syndrome and, similarly to other studies in non-white populations, this study finds a considerable classification disagreement between the definitions [2,8]. Only few prospective surveys have addressed the relationship between the metabolic syndrome and subsequent CVD, and the results are inconsistent [10–12]. Although the two syndromes agree in their focus on obesity, dyslipidaemia, hypertension, and glucose intolerance as constituent traits, it is obvious that the different definitions and approaches account for much of the differences in prevalence estimates and the differences in the impact on incident diabetes and CVD observed in prospective studies. The way that both definitions weigh each component in the syndrome equally and independently may cause a substantial lack of sensitivity and specificity in detecting future CVD; and it remains to be explored whether this dichotomization of metabolic risk is appropriate for prediction of disease. The question is whether the metabolic syndrome increases risk for adverse outcomes to a greater degree than predicted by the presence of its individual components. Validated CVD risk score programmes such as the Framingham risk score or the Precard Programme® may provide better estimates of future CVD [13,14].

Although the two different approaches—the physiological vs. the epidemiological—may lead to some confusion, there are also rational aspects to it. From a physiological perspective a better understanding of the impact and consequences of insulin resistance is highly relevant. For the sake of comparability of future studies, common standards for methodologies and definitions of the syndrome are needed. In public health and preventive medicine a more pragmatic approach is needed. Here the primary goal of identifying metabolic risk factors is to prevent morbidity and mortality due to Type 2 diabetes and CVD. Thus easily applicable definitions or risk scores adjusted to specific ethnic groups are needed. However, in this perspective, interventions to decrease obesity and improve physical activity behaviour will probably be the greatest benefit of the current focus on the metabolic syndrome.

Marit Eika Jørgensen and Knut Borch-Johnsen*
*National Public Health Institute, Section for Research in Greenland, Copenhagen, and *Steno Diabetes Centre, Gentofte, Denmark*

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