EDITORIAL COMMENT

Metabolic syndrome: What is it and how useful is the diagnosis in clinical practice?

Síndrome metabólica: a sua existência e utilidade do diagnóstico na prática clínica

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Concept

The metabolic syndrome (MS) has been recognized for several decades, although under different names and with different definitions, but in recent years controversy has arisen concerning its definition and significance.\(^1,2\) The term does not refer to a specific disease, but to a cluster of metabolic risk factors that tend to occur together: central (or abdominal) obesity, elevated triglycerides, low HDL cholesterol, glucose intolerance and hypertension. It is thus not a genuine clinical entity caused by a single factor, but varies in its components between individuals, particularly between different ethnic groups. Although the concept is well established, there are differences in the criteria for a diagnosis of MS published by various organizations, including the World Health Organization (WHO), the European Group for Study of Insulin Resistance (EGIR), the International Diabetes Federation (IDF), the National Cholesterol Education Program Third Adult Treatment Panel (NCEP-ATP III), the American Diabetes Association (ADA) and the American Association of Clinical Endocrinologists (AACE). Out of this disagreement came a consensus on a worldwide definition of MS published by various organizations, including the World Health Organization (WHO), the European Group for Study of Insulin Resistance (EGIR), the International Diabetes Federation (IDF), the National Cholesterol Education Program Third Adult Treatment Panel (NCEP-ATP III), the American Diabetes Association (ADA) and the American Association of Clinical Endocrinologists (AACE). Published in 2009.\(^3\) The main difference between the IDF and NCEP-ATP III definitions of MS was in the cutoff used for waist circumference,\(^4,5\) but a single overall value is no longer obligatory, and national or regional cutoffs for waist circumference can be used. In this worldwide definition, the criteria for the clinical diagnosis of MS are: elevated waist circumference (population- and country-specific definitions); elevated triglycerides (≥150 mg/dl) or under drug treatment with fibrates or nicotinic acid or taking high-dose omega-3 fatty acids; reduced HDL cholesterol (<40 mg/dl in males and <50 mg/dl in females) or under drug treatment with fibrates or nicotinic acid; elevated blood pressure (systolic ≥130 and/or diastolic ≥85 mmHg) or under antihypertensive therapy; and elevated fasting glucose (≥100 mg/dl) or under antidiabetic medication. Nevertheless, the definition of MS is not fully harmonized.\(^6\)

Prevalence

The prevalence of MS varies according to age, gender, ethnic origin and the definition used.\(^7–10\) The IDF/AHA/NHLBI criteria being more sensitive than those of the NCEP-ATP III in identifying MS.\(^9,10\) The prevalence is lower in adolescents than in young adults and the elderly; and lower in males.\(^7–9,12\) However, it is estimated that 20–30% of adults in most countries could be considered to have MS.\(^11,13\)

Risk

It is accepted that individuals with MS are more prone to diabetes and cardiovascular disease.\(^14\) A recent meta-analysis shows that in those with MS according to the 2001
NCEP-ATP III criteria and the revised 2004 criteria, the relative risk of cardiovascular events and death is 2 and 1.5, respectively. However, most studies indicate that the ability of the syndrome to predict cardiovascular events or disease progression is no greater than that based on the sum of its components. On the other hand, a meta-analysis published in 2006 showed increased risk after adjustment for traditional cardiovascular risk factors; the association was stronger in women, in individuals at lower risk (<10%) and in studies based on the WHO definition rather than the NCEP-ATP III or other definitions. In this meta-analysis the risk associated with MS was greater than the sum of its components, but the question of whether MS is a better predictor of risk than traditional risk factors remains the subject of debate.

Causes

The pathogenesis of MS and of each of its components is not fully understood, but central obesity and insulin resistance are the most important variables in its expression. Excessive visceral adiposity triggers the onset of MS, leading to hyperinsulinemia which may not cause raised fasting or postprandial glucose for years, so long as beta cells continue to respond. However, in genetically predisposed individuals these alterations occur as a result of impaired insulin secretion or reduced glucose tolerance. This pathogenic mechanism, insulin resistance (which is difficult to assess in routine clinical practice), and the inflammatory process triggered by obesity, underlie virtually all aspects of MS. Adipose tissue dysfunction lies behind the risk arising from visceral obesity, which is associated with atherogenic dyslipidemia (raised triglycerides, low HDL cholesterol, and raised ApoB, small dense LDL particles and small HDL particles), endothelial dysfunction and hypertension. 

Metabolic and pathological factors other than obesity also play a part in this complex process: inflammatory factors, adipocytokines (leptin, adiponectin, resistin), cortisol, oxidative stress, vascular factors, heredity and lifestyle. Not all can be explained by genetics, since the prevalence of MS has risen in recent years but the human genetic profile has not changed. This suggests that the interaction of environmental factors with genetic predisposition leads individuals with MS to accumulate energy in the form of fat. The most likely culprits are excessive consumption of high-energy foods, especially saturated fats, and sedentary lifestyles, all influenced by various factors related to the home, transport, and the workplace.

Prevention and treatment

The evidence indicates that individuals with MS have high cardiovascular risk. The hypothesis that MS results from insulin resistance points the way to a control strategy; since weight loss frequently reduces insulin resistance, measures that can be adopted to prevent and treat MS include a healthy, low-energy diet together with regular exercise and possibly other measures such as bariatric surgery. Besides, there are currently no drugs that can modulate the mechanisms underlying MS as a whole and reduce the metabolic and cardiovascular effects of the associated risk factors. In individuals in whom lifestyle modification has been insufficient and who are considered at high cardiovascular risk, the residual risk may justify using appropriate therapies to control glucose metabolism abnormalities, lipid disorders and hypertension.

To summarize, clinicians should treat individuals with MS as a high-risk group and advise them to adopt a healthy lifestyle, while estimating their overall risk with a view to prescribing the therapies recommended for cardiovascular prevention in clinical practice. The study by Rossa et al. in this issue of the Journal aimed to determine the prevalence of MS and to identify variables related to its development in a population of hospital workers in Porto Alegre, Brazil. The methodology was that of a cross-sectional study, in which a representative sample of the target population was analyzed, selected on the basis of an estimated MS prevalence of 25%, a figure in agreement with the literature. Components of MS and variables related to its clinical consequences (diabetes and cardiovascular disease) were excluded from the multivariate analysis. Since one aim of the study was to identify socioeconomic, demographic and occupational factors related to the development of MS, it was necessary to control for variables that are part of its definition. The figure for MS prevalence determined by the study (13%) was lower than estimated, but this is due to the participants' relatively young mean age (35 years). It is also not surprising that this figure is lower than in another Brazilian study with a similarly sized sample but of cardiological outpatients (62% in men and 65% in women), and lower than in population studies in Portugal – 27% in a population with a mean age of 59 and 24% in a national survey (mean age 58). The higher prevalence of MS in those with a lower educational level is noteworthy; this is further evidence of an environmental component in the pathogenesis of MS interacting with genetic factors.

The literature on MS is vast and there is still disagreement concerning both its definition and its prevalence. It should be borne in mind that MS prevalence depends on methodological aspects of sampling and diagnosis, and so comparative studies are often of limited value. At all events, MS is common, and is considered a high-risk obesity state. At the same time, as obesity increases in the young, the prevalence of MS is also set to rise. Strategies should therefore be defined to raise awareness in different population groups, from schools to the workplace. It is essential to prevent obesity by adopting healthy eating habits and taking regular exercise to lose weight or to avoid weight gain. If this behavioral component is not effectively modified, the result will be an increasingly medicated society. To avoid this scenario, it will be necessary to involve health professionals, educators, organizations working in health-related areas, political decision-makers and public health authorities, since the metabolic syndrome is beginning to take on the dimensions of a pandemic.

Conflicts of interest

The author has no conflicts of interest to declare.
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References


