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Review article

The metabolic syndrome: A vascular perspective

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Abstract

The metabolic syndrome (MS) is a clustering of cardiovascular risk factors. Current definitions of MS use hypertension, waist circumference, fasting glucose, triglyceride and HDL-cholesterol levels as defining variables. The prevalence of MS is increasing in our society due to lifestyle changes that result in decreased physical activity and increased body weight. Patients with MS have a three times greater risk of coronary heart disease and stroke, and a two to four times greater risk of dying from atherosclerotic coronary heart disease than those without MS. Imaging studies have shown an increased burden and progression of atherosclerosis. Also, MS patients seem to be more vulnerable to events at comparable levels of atherosclerosis. First-line treatment for MS is therapeutic lifestyle intervention, including exercise and weight reduction. Medical intervention strategies using blood pressure-lowering medication, statins, fibrates and metformin seem the most appropriate to date. The effects of thiazolidinediones on cardiovascular endpoints have not been studied to a large extent in the setting of MS. Evidence regarding risk assessment and optimal medical strategies will be an important aspect of vascular research in the coming years.

Keywords: Metabolic syndrome; Atherosclerosis; Cardiovascular disease

Contents

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1. Introduction

In addition to the classic cardiovascular risk factors, the metabolic syndrome (MS)–a clustering of cardiovascular risk factors [1,2]–is increasingly being recognized as an important factor in the pathophysiology of atherosclerosis and as a target of therapy [3]. MS is closely related to present-day changes in lifestyle and their ensuing consequences, such as a lack of physical activity and an increase in body weight. The prevalence of MS has exceeded 20% of the adult population in many countries and is still increasing [4].

Because MS is defined as a clustering of risk factors, some have argued that MS-associated cardiovascular risk is nothing more than the sum of the risks of its defining components. Intriguingly, combinations of risk factors seem to enhance each other. This has been shown in MS, as the syndrome more strongly predicted mortality than did its individual components [5]. Another example of risk enhancement was recently observed for nine environmental risk factors, several reminiscent of MS [6]. In this article, we will address MS from a vascular perspective.

2. The metabolic syndrome: definition and criteria

MS has been defined by the WHO, the American National Cholesterol Education Program (NCEP) and the European Group for the Study of Insulin Resistance (EGIR) [3,7,8]. The EGIR definition is a specification of the WHO classification system. MS is defined as a sum of the criteria listed in Table 1. The "calculation rules" used in the different classifications are as follows:

1. WHO/EGIR: the presence of impaired fasting glucose or insulin resistance is a *prerequisite* for the definition. In addition, two or more criteria have to be present.
2. NCEP: three or more criteria are present.

A patient can thus be classified or diagnosed as having MS (ICD code: 277.7 [9]). The discussion and studies comparing the classification systems [10–15] in order to assess which one to follow in daily practice is beyond the scope of this review. Given the emerging central role for abdominal adiposity [16–19], this risk factor will be discussed in some detail. The other criteria will be mentioned only briefly.

2.1. Impaired fasting glucose (IFG)

Fasting glucose levels of 5.6 to 5.9 mmol/L have recently been proposed as the cut-off point for IFG as this predicts future diabetes most precisely [20]. The classification systems have not yet adopted this criterion [21] for MS, although the discussion is ongoing [22].

2.2. Insulin resistance or hyperinsulinemia

This aspect is regarded by some as a pathophysiologic key to the metabolic and vascular changes of MS. Insulin has vasoactive properties. Furthermore, hyperinsulinemia has

Table 1
Criteria and definition of the metabolic syndrome

Criteria of the metabolic syndrome		NCEP/ATP III [3]	EGIR-modified WHO [7,8]
Glucose	fasting	>6.1 mmol/L	>6.1 mmol/L or DM
Insulin	fasting	–	Upper 25% normal
	resistance		Lowest 25% "QUICKI"
Visceral obesity	♂ waist girth	>102 cm (>94 cm)*	≥94 cm
	♂ WHR	–	≥0.91
	♀ waist girth	>88 cm	≥80 cm
	♀ WHR	–	≥0.86
Triglycerides		>1.7 mmol/L	>1.7 mmol/L
HDL-cholesterol	♂	<1.0 mmol/L	<0.9 mmol/L
	♀	<1.3 mmol/L	<1.0 mmol/L
Blood pressure		≥130/≥85 mm Hg	≥140/≥90 mm Hg (WHO ≥160/90)
Microalbuminuria		No	No (WHO yes)
Definition of the metabolic syndrome		The presence of 3 or more of the criteria listed above	Hyperinsulinemia, IGT or diabetes and 2 or more of the criteria listed above

Some male patients can develop multiple metabolic risk factors when the waist circumference is only marginally increased. Such patients may have a strong genetic contribution to insulin resistance [3].