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EDITORIAL

Metabolic syndrome and peripheral arterial disease



Síndrome metabólico y enfermedad arterial periférica

The metabolic syndrome (MetS) is a constellation of metabolic risk factors closely linked to insulin resistance.¹ At present, various definitions for MetS are used. According to the criteria described by of the Adults Treatment Panel III recently revised by the American Heart Association/National Heart, Lung, and Blood Institute (rATP III-MetS)² the MetS is defined as an alteration in three or more of the following features: abdominal obesity (waist circumference >102 cm in men; >88 cm in women), elevated blood pressure (>130 mmHg systolic or >85 mmHg diastolic, and/or use of antihypertensive agents), hypertriglyceridemia (>150 mg/dL), low levels of serum HDLc (<40 mg/dL in men, <50 mg/dL in women), and high fasting glucose (>100 mg/dL, and/or use of glucose-lowering agents). Using International Diabetes Federation (IDF) criteria,³ MetS was diagnosed in patients who had a waist circumference >94 cm in men and >80 cm in women, plus two or more of the following: elevated blood pressure, hypertriglyceridemia, low HDLc levels, and high fasting glucose, each defined by the same criteria used for the rATP III definition. Diabetes mellitus was defined as fasting plasma glucose >126 mg/dL or use of glucose-lowering agents. MetS is a very common clinical condition in Western countries: in the last decade, the prevalence of MetS has increased in the United States⁴ and elsewhere. In people >20 years old it is 24% and it rises to >40% in patients \geq 60 years of age.⁵ Several studies evaluated the presence of the Mets in different populations. However, the use of different diagnostic criteria for the Mets is, at least in part, the reasons for differences in prevalence rate, hindering meaningful comparisons between populations.^{6,7} In a study by Trevisan et al., in patients aged 50 years or above, women showed a higher prevalence than men,⁸ although the prevalence of the Mets was not influenced by age. The pathogenesis of the syndrome has multiple origins, but obesity and sedentary lifestyle coupled with diet

and still largely unknown genetic factors clearly interact and may determine the syndrome.⁹ The combination of risk factors comprising the Mets interacts synergistically causing or accelerating the progression of atherosclerosis.¹ Several clinical studies recognized MetS as a cause responsible for the endothelial dysfunction, which represents the first “step” in atherothrombotic disease and, in addition, observed an association between increased carotid intima-media thickness (IMT) and MetS.^{10,11} Therefore, patients with Mets have a higher risk of developing cardiovascular morbidity and mortality than subjects without the syndrome (12.0% versus 2.2%): a two- to three-fold increased risk of coronary heart disease (CHD) and stroke and cardiovascular mortality has been reported in literature.^{1,6,8,12} A prospective study published by Novo et al. showed that in the subgroup of patients with MetS, the prevalence of subclinical atherosclerosis, defined as increased IMT (common carotid IMT > 0.90 mm) with or without atherosclerotic plaque, was significantly higher than in participants without MetS and defined this Syndrome as a CV risk factor: participants with MetS had a significantly higher prevalence of vascular disease in a 20-year follow-up (49%) than participants without MetS (29%) ($p < 0.01$).^{9,13} Conversely, little is known about the predictive role of MetS in peripheral arterial disease (PAD), which affecting about 27 million people in Europe and the United States. Brevetti et al. found that more than 50% of PAD patients met the criteria for rATP III-MetS. Nevertheless, the results show that IDF-METs, but not rATP III-MetS, is an independent predictor of cardiovascular events.¹⁴ In a study by Gorter et al. has emerged that the metabolic syndrome, according to the ATP III criteria, is highly prevalent in patients with a recent diagnose of a clinical manifestation of atherosclerosis (46%), especially in PAD patients (58%).¹⁵ A more recent study revealed that patients with occlusive or aneurysmatic PAD have a high prevalence of metabolic syndrome and that in both groups of patients the presence of metabolic syndrome was independently associated with an increased risk for the occurrence of CV events during long-term follow-up but no with an incremental risk for CV mortality.¹⁶ The Mets is a common comorbidity in claudicants

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and must be actively searched because the early diagnosis and treatment of MetS may influence PAD progression.¹⁷ There are few studies in literature which evaluated the association between MetS and PAD. These studies demonstrated that the prevalence of MetS is higher in patients with PAD but their limits were that the patients often exhibited clinical manifestations of arteriosclerosis in other vascular territories.¹⁴⁻¹⁷ In this regard the objective of the *study presented in this issue of Rev Clin Esp* by Estirado et al.¹⁸ is to assess the prevalence of MetS in patients with PAD but without known atherosclerosis in other districts. The authors demonstrated that the prevalence of MetS in PAD patients is high (63%) and is independent of the evolution time of PAD. According to our experience we are agree with Estirado et al.¹⁸; we believe that PAD (documented using ABI <0.9, lower limb amputation due to chronic ischemia or prior revascularization in the lower limbs), can be presented in MetS patients and that it is a validated marker of subclinical atherosclerosis and a predictor of CV events, like an increased carotid IMT.

Considering the close association between MetS and GCVR (global cardiovascular risk), it is relevant to screen already high-risk patients for the MetS. Instead of treating individual components of the metabolic syndrome, treating the underlying pathophysiological disturbance (for instance, insulin resistance) would ideally be the therapeutic option of first choice.¹⁵ It is also recommend preventing the development of MetS abnormalities (for example with daily physical activity, Mediterranean diet and early started pharmacological treatment of modifiable risk factors, as suggested by many studies)^{19,20} and investigating the presence of subclinical atherosclerosis in all patients over 45 years, by ultrasound test, because in primary prevention, the IMT measurement can give further information for a better stratification of GCVR.²¹

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