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EDITORIAL COMMENT

Cystatin C: An underexplored biomarker that goes beyond renal function

Cistatina C: um biomarcador por explorar que vai para além da função renal

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The metabolic syndrome (MetS) is a multiplex risk factor that consists of several risk correlates of metabolic origin. In addition to atherogenic lipid profile, hypertension, glucose intolerance and abdominal obesity, the syndrome carries a prothrombotic and a proinflammatory state. Persons with the MetS are at essentially twice the risk for cardiovascular disease compared with those without the syndrome. It further raises the risk for type 2 diabetes about five-fold.[1] Although there is still a lack of clarity in the definition of MetS (the National Cholesterol Education Program – Adult Treatment Panel III and the International Diabetes Federation use different criteria), the key clinical implication of a diagnosis of the syndrome is to decrease associated morbidity and mortality, through identification and management of its individual components.[2] MetS is becoming increasingly common, affecting approximately 20–30% of the adult population in most countries.[3] Age, race and increased body weight, as well as socioeconomic and lifestyle factors such as diet, smoking, soft drink consumption and physical inactivity, are associated with an increased risk of MetS.[4]

Although the exact mechanism underlying MetS has not yet been fully elucidated, many studies have shown that it is strongly associated with inflammation, insulin sensitivity, endothelial dysfunction, renal dysfunction and oxidative stress. As a result, several biological markers have been identified as risk factors for cardiovascular disease and are associated with increased risk of MetS.[5]

The level of cystatin C (CysC) in the bloodstream has been used clinically mainly as a biomarker of glomerular filtration and early renal dysfunction. However, recent reports suggest that CysC can predict cardiovascular risk through atherosclerosis and obesity, independently of renal function.[6] Serum CysC is elevated in obese subjects of both genders, independently of reduced estimated glomerular filtration rate (eGFR).[7] Besides reduced eGFR and adiposity, several other factors are known to influence circulating CysC concentrations, including older age.

In a recent study, CysC was measured in 1502 individuals included in the Malmö Diet and Cancer cardiovascular cohort who were free from MetS at baseline and subsequently underwent a follow-up examination after a median of 16 years. During follow-up, 428 subjects developed new-onset MetS. The only MetS component prospectively significantly associated with increased baseline CysC levels was the incidence and long-term progression of abdominal obesity, indicating that the association between CysC levels and incident MetS might be mediated to a large extent by visceral fat.[8]

In this issue of the *Journal*, Ping Liu et al. of Shandong University present an article entitled ''Clinical analysis of the relationship between cystatin C and MetS in the elderly''.[9] The authors studied 380 elderly individuals divided into three groups: (1) patients with MetS (n=135); (2) patients without MetS but with at least one diagnostic

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criterion of MetS (n=142); and (3) a control group of healthy elderly persons (n=103). Several variables related to weight, lipid profile, glucose metabolism and blood pressure were obtained, as well as measurement of CysC, serum creatinine and microalbuminuria. The authors concluded that CysC was significantly associated with MetS in the elderly and that as MetS scores rose, serum CysC levels increased. One of the limitations of the study pointed out by the authors in the discussion is the non-inclusion of inflammatory variables. A number of recent studies have demonstrated a correlation between inflammatory mediators and MetS components, and an association between inflammatory markers and the severity of MetS has also been reported.[10] These indicators of inflammation in MetS may be early markers of the development of CVD.

In a recent analysis of the prospective Multiethnic Study of Atherosclerosis cohort which included 6814 men and women aged 45–84 years old followed for a period of 5.5 years, Agarwal et al. examined the joint association of chronic kidney disease (CKD) and MetS with incident cardiovascular disease (CVD). They demonstrated that CKD and MetS were independent predictors of CVD (hazard ratio, 2.02 for CKD, and 2.55 for MetS), with an additive interaction of CKD and MetS (adjusted HR for the CKD+/MetS+ group 5.56 compared to the CKD−/MetS− group).[11]

The most important merit of the study by Ping Liu et al.[9] is to draw attention to the expanded role of serum cystatin C levels beyond estimation of renal function. Although more research is needed, cystatin C appears to be of value in the cardiovascular risk stratification of elderly patients with MetS or even with only some of the components of its diagnostic criteria.

Conflicts of interest

The author has no conflicts of interest to declare.

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