Association of metabolic syndrome with coronary artery calcification

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Metabolic syndrome (MetS) is a cluster of metabolic disorders defined by a combination of obesity, insulin resistance, glucose intolerance, dyslipidemia, and hypertension. Globally, the prevalence of MetS is increasing, and the same trend is occurring in Korea. According to data from the Korea National Health and Nutrition Examination Survey, the age-adjusted prevalence of MetS increased from 19.6% in 1998 to 32.4% in 2007 to 2009 [1].

MetS has been defined differently by the World Health Organization (WHO), European Group for the Study of Insulin Resistance (EGIR), National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III), and International Diabetes Federation (IDF). Each definition includes similar components, but the cutoff values differ slightly. For instance, the EGIR regards hyperinsulinemia and insulin resistance as a mandatory component of MetS, while the IDF focuses on waist circumferences as a marker of abdominal obesity [2]. Accordingly, several studies have shown that there is considerable variability in the identification of MetS [3,4].

MetS confers high risks of coronary artery disease (CAD), stroke, and cardiovascular mortality [5]. Some studies have compared the definitions of MetS in terms of impact on cardiovascular disease (CVD) events. The effects of MetS on CVD events were similar, despite differences in prevalence among definitions [6-8]. By contrast, the Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe (DECODE) project reported that the WHO definition resulted in a higher risk of cardiovascular mortality in males, compared with other definitions [9]. In the Strong Heart Study, the WHO definition was a better predictor of CVD than the NCEP ATP III and IDF definitions in participants with diabetes, although there was no significant difference in nondiabetic participants [10].

Coronary artery calcium (CAC) on computed tomography (CT) has been evaluated as a non-invasive measurement for detecting subclinical atherosclerosis and CAD. Several studies have explored the association of MetS with subclinical atherosclerosis, defined by CAC, in general populations. Wong et al. [11] reported that persons with MetS had a 1.4-fold increased risk of the presence of CAC, compared with those without MetS. In addition, in the MESA study, the relative risk for incident CAC was 7.8 for subjects with MetS, compared with those without
MetS and diabetes [12]. It was also shown that when CAC was not increased, the risks of cardiovascular morbidity and mortality were low in persons with MetS or diabetes [13]. Few studies have compared the definitions of MetS in terms of the impact on atherosclerosis. Narla et al. [14] compared three definitions of MetS (NCEP ATP III, American Heart Association/National Heart, Lung, and Blood Institute, and IDF) in terms of the CAC score, and found no difference according to the definition used.

The mechanism of the link between MetS and increased CAD risk remains uncertain. However, central obesity and insulin resistance might have major roles in the association (Fig. 1). Adipose tissue releases non-esterified fatty acids, plasminogen activator inhibitor-1, inflammatory cytokines (e.g., tumor necrosis factor-α, interleukin 6, angiotensin 2, neprilysin, visfatin, and fibroblast growth factor 21), and adipocytokines (e.g., adiponectin, leptin, and resistin). These adipose tissue products play important roles in the pathogenesis of glucose and lipid metabolic disorders (elevated triglyceride levels, small low density lipoprotein (LDL) and very low density lipoprotein (VLDL) particles, and low high density lipoprotein cholesterol (HDL-C) levels), insulin resistance, and thrombogenic cardiovascular events. In addition, obesity is associated with hypertension and hyperglycemia, which might promote atherosclerosis [15,16]. Insulin resistance is associated with the hepatic production of VLDL particles and an atherogenic lipoprotein profile involving low HDL-C levels and elevated small LDL particle levels, and increased peripheral vasoconstriction and sodium retention by causing hyperinsulinemia and hyperglycemia [17].

In this issue of The Korean Journal of Internal Medicine, Seo et al. [18] investigated the association of MetS and components of MetS with CAC, a marker of coronary atherosclerosis, and evaluated differences in the effect according to different definitions of MetS in a hospital-based cohort study. Each definition of MetS was significantly associated with the presence of CAC after adjusting for confounders such as age, gender, hypertension, diabetes mellitus, LDL-cholesterol, smoking status, and exercise. Moreover, a higher number of MetS components was significantly associated with a higher risk of CAC. However, there was no difference according to the definition of MetS used.

The strengths of this study are the large sample size and standardized protocol. However, it has some limitations. The study was cross-sectional, so we cannot draw conclusions about causality. In addition, a previous study reported that MetS is related to the incidence or progression of CAC [12]. However, Seo et al. [18] did not consider changes in CAC. Lastly, this study did not consider all possible definitions of MetS because of the limited parameters.

In conclusion, MetS, including obesity and insulin resistance, is significantly associated with the development of subclinical atherosclerosis. The early detection of subclinical atherosclerosis is important and CAC on CT is a good tool for the early detection of subclinical CAD. Prospective studies are needed to determine the relationship of MetS with the future incidence of CAC and CAD events.

Conflict of interest
No potential conflict of interest relevant to this article was reported.

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