EDITORIAL

Korean J Intern Med 2015;30:29-31
http://dx.doi.org/10.3904/kjim.2015.30.1.29

KJIM

Association of metabolic syndrome with coronary artery calcification

Kyoung Hwa Ha[1] and Dae Jung Kim[1,2]

[1]Cardiovascular and Metabolic Disease Etiology Research Center, [2]Department of Endocrinology and Metabolism, Ajou University School of Medicine, Suwon, Korea

See Article on Page 73-81

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. A meta-analysis showed that individuals with MetS are at 2-fold greater risk of myocardial infarction, 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

Received: December 11, 2014
Accepted: December 16, 2014

Correspondence to
Dae Jung Kim, M.D.
Department of Endocrinology and Metabolism, Ajou University School of Medicine, 164 World cup-ro, Yeongtong-gu, Suwon 443-380, Korea
Tel: +82-31-219-5128
Fax: +82-31-219-7464
E-mail: djkim@ajou.ac.kr

pISSN 1226-3303
eISSN 2005-6648
http://www.kjim.org

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].

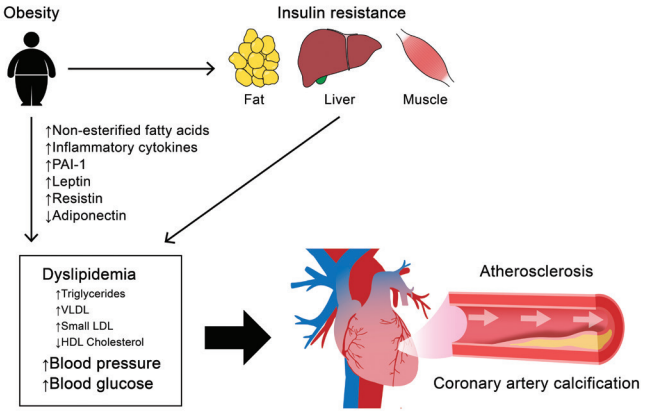

Figure 1. Proposed mechanism for the link between metabolic syndrome and coronary arterial calcification. PAI-1, plasminogen activator inhibitor-1; VLDL, very low density lipoprotein; LDL, low density lipoprotein; HDL, high density lipoprotein.

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.

Acknowledgments

This study was supported by a grant of the Korean Health Technology R&D Project, Ministry of Health and Welfare, Republic of Korea (HI13C0715).

http://dx.doi.org/10.3904/kjim.2015.30.1.29

REFERENCES

1. Oh SW. Obesity and metabolic syndrome in Korea. Diabetes Metab J 2011;35:561-566.
2. Kassi E, Pervanidou P, Kaltsas G, Chrousos G. Metabolic syndrome: definitions and controversies. BMC Med 2011;9:48.
3. Alberti KG, Zimmet P, Shaw J. Metabolic syndrome: a new world-wide definition: a consensus statement from the International Diabetes Federation. Diabet Med 2006;23:469-480.
4. Kim HC, Kim DJ. Causes of different estimates of the prevalence of metabolic syndrome in Korea. Korean J Intern Med 2011;26:440-448.
5. Mottillo S, Filion KB, Genest J, et al. The metabolic syndrome and cardiovascular risk a systematic review and meta-analysis. J Am Coll Cardiol 2010;56:1113-1132.
6. Benetos A, Thomas F, Pannier B, Bean K, Jego B, Guize L. All-cause and cardiovascular mortality using the different definitions of metabolic syndrome. Am J Cardiol 2008;102:188-191.
7. Mancia G, Bombelli M, Facchetti R, et al. Impact of different definitions of the metabolic syndrome on the prevalence of organ damage, cardiometabolic risk and cardiovascular events. J Hypertens 2010;28:999-1006.
8. Nilsson PM, Engstrom G, Hedblad B. The metabolic syndrome and incidence of cardiovascular disease in non-diabetic subjects: a population-based study comparing three different definitions. Diabet Med 2007;24:464-472.
9. Qiao Q; DECODE Study Group. Comparison of different definitions of the metabolic syndrome in relation to cardiovascular mortality in European men and women. Diabetologia 2006;49:2837-2846.
10. de Simone G, Devereux RB, Chinali M, et al. Prognostic impact of metabolic syndrome by different definitions in a population with high prevalence of obesity and diabetes: the Strong Heart Study. Diabetes Care 2007;30:1851-1856.
11. Wong ND, Sciammarella MG, Polk D, et al. The metabolic syndrome, diabetes, and subclinical atherosclerosis assessed by coronary calcium. J Am Coll Cardiol 2003;41:1547-1553.
12. Wong ND, Nelson JC, Granston T, et al. Metabolic syndrome, diabetes, and incidence and progression of coronary calcium: the Multiethnic Study of Atherosclerosis study. JACC Cardiovasc Imaging 2012;5:358-366.
13. Malik S, Budoff MJ, Katz R, et al. Impact of subclinical atherosclerosis on cardiovascular disease events in individuals with metabolic syndrome and diabetes: the multi-ethnic study of atherosclerosis. Diabetes Care 2011;34:2285-2290.
14. Narla V, Santos RD, Campbell CY, et al. Coronary artery calcification and inflammation according to various metabolic syndrome definitions. J Cardiometab Syndr 2009;4:33-39.
15. Grundy SM. Obesity, metabolic syndrome, and cardiovascular disease. J Clin Endocrinol Metab 2004;89:2595-2600.
16. Stevenson JE, Wright BR, Boydstun AS. The metabolic syndrome and coronary artery disease: a structural equation modeling approach suggestive of a common underlying pathophysiology. Metabolism 2012;61:1582-1588.
17. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet 2005;365:1415-1428.
18. Seo MH, Rhee EJ, Park SE, et al. Metabolic syndrome criteria as predictors of subclinical atherosclerosis based on the coronary calcium score. Korean J Intern Med 2015;30:73-81.