Relations between microvascular function and aortic stiffness in metabolic syndrome

Metabolik sendromda mikrovasküler fonksiyon ve aort sertliği arasındaki ilişki

The metabolic syndrome (MetS) is characterized by abdominal obesity, elevated blood pressure, hypertriglycemia, low high-density lipoprotein (HDL) cholesterolemia, and hyperglyceridmia (1). Vascular dysfunction caused by endothelial dysfunction is an early abnormality in the MetS that may contribute to premature atherosclerosis (2). Each of the components of the MetS has been independently associated with vascular dysfunction (3-5). Because there was the 2.6-fold increased risk of coronary death among those with the MetS (6), other mechanisms may contribute to the potential adverse effect of features of the MetS on vascular function and, in particular, endothelial function, thereby increasing the potential for atherothrombotic complications (7). Several studies demonstrated the relationship between MS and coronary microvascular circulation. MetS patients showed impaired response of myocardial blood flow to a cold press or test in by PET analysis (8), indicating the presence of coronary microvascular endothelial dysfunction. Similarly, MetS patients showed an impaired coronary blood flow in with angiographically normal coronary arteries by Thrombolysis in Myocardial Infarction frame count method (9). Moreover, patients with MetS showed an impaired vasodilatory response to pharmacologic agents in the left ascending of coronary artery by transthoracic echocardiography (10). Possible mechanisms for impaired coronary vasodilation in patients with MetS are insulin resistance which may induce endothelial dysfunction mediated by oxidative stress (11), reduced adiponectin which have a role in the phosphorylation of eNOS (12), release of pro-inflammatory cytokines (e.g., interleukin-6, tumor necrosis factor-α) by visceral adipose tissue (13). These mechanisms may solely and/or multifactorially contribute to coronary endothelial dysfunction in MetS patients (14).

The present study revealed that coronary flow reserve (CFR) is impaired in patients with MetS and there is an independent relationship between impaired CFR and increased aortic stiffness evaluated by echocardiography. This study demonstrates that CFR was significantly correlated with age, blood pressure, waist circumference, lipid profile, fasting glucose, high-sensitivity C-reactive protein, left ventricular (LV) mass index , and aortic stiffness. The relationship between CFR and aortic stiffness persisted after adjusting for age and each components of MetS.

In this study, the evaluation of aortic stiffness was performed via relating change in diameter of aorta to distending pressure, not assessed by pulse wave velocity (PWV) (15). In previous studies, significant correlations between CFR and aortic stiffness assessed by PWV have been demonstrated in patients with hypertension and coronary artery disease. PWV is the gold standard of aortic stiffness and easily performed in clinical practice. To prove the efficacy of newly non-invasive method to detect the aortic stiffness, the description of the method is needed, but the authors did not describe the methodological review of aortic stiffness. Moreover, the hypothesis that coronary flow may be influenced by aortic elastic properties was not confirmed by simply demonstrating the relationship between CFR and aotrtic stiffness. Because increased left ventricular (LV) end diastolic pressure associated with LV hypertrophy and endothelial dysfunction may interacts with aortic stiffness and CFR in MetS, further evaluations such as LV filling pressure and brachial flow-mediated dilatation, which was associated with aortic stiffness in the Framingham Heart Study offspring cohort (16) are needed.

However, the finding of impaired coronary microvascular dysfunction is more prominent in MS patients may provide important information clarifying the pathogenesis of MetS-induced cardiovascular events. Moreover, further evidence is needed for the early presence of impaired endothelium-independent and endothelium-dependent coronary vasodilator function in patients with MetS and if these abnormalities in coronary vasodilator function are worsened by the combined presence of already-established cardiovascular risk factors (i.e., dyslipidemia, smoking, and CAD).

Tae Joon Cha, Kyoung Im Cho
Division of Cardiology, Department of Internal Medicine, Kosin University School of Medicine, Busan-*South Korea*

Conflict of interest: None declared.

Address for Correspondence/Yazışma Adresi: Dr. Tae Joon Cha, Division of Cardiology, Department of Internal Medicine, Faculty of Medicine, Kosin University, 34 Amnam-Dong Seo-Ku, Busan 602-702-*South Korea* E-mail: chatjn@hanafos.com
Accepted Date/Kabul Tarihi: 11.01.2013 **Available Online Date/Çevrimiçi Yayın Tarihi:** 06.02.2013

doi:10.5152/akd.2013.069

References

1. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation 2002; 106: 3143-421.
2. Watarai T, Yamasaki Y, Ikeda M, Kubota M, Kodama M, Tsujino T, et al. Insulin resistance contributes to carotid arterial wall thickness in patients with non-insulin-dependent-diabetes mellitus. Endocr J 1999; 46: 629-38. [CrossRef]
3. Pitkänen OP, Nuutila P, Raitakari OT, Porkka K, Iida H, Nuotio I, et al. Coronary flow reserve in young men with familial combined hyperlipidemia. Circulation 1999; 99: 1678-84. [CrossRef]
4. Di Carli MF, Janisse J, Grunberger G, Ager J. Role of chronic hyperglycemia in the pathogenesis of coronary microvascular dysfunction in diabetes. J Am Coll Cardiol 2003; 41: 1387-93. [CrossRef]
5. Schindler TH, Cardenas J, Prior JO, Facta AD, Kreissl MC, Zhang XL, et al. Relationship between increasing body weight, insulin resistance, inflammation, adipocytokine leptin, and coronary circulatory function. J Am Coll Cardiol 2006; 47: 1188-95. [CrossRef]
6. Rewers M, Zaccaro D, D''Agostino R, Haffner S, Saad MF, Selby JV, et al. Insulin sensitivity, insulinemia, and coronary artery disease: the Insulin Resistance Atherosclerosis Study. Diabetes Care 2004; 27: 781-7. [CrossRef]
7. Forgione MA, Leopold JA, Loscalzo J. Roles of endothelial dysfunction in coronary artery disease. Curr Opin Cardiol 2000; 15: 409-15. [CrossRef]
8. Quiñones MJ, Hernandez-Pampaloni M, Schelbert H, Bulnes-Enriquez I, Jimenez X, Hernandez G, et al. Coronary vasomotor abnormalities in insulin-resistant individuals. Ann Intern Med 2004; 140: 700-8.
9. Turhan H, Erbay AR, Yaşar AS, Biçer A, Şaşmaz H, Yetkin E. Impaired coronary blood flow in patients with metabolic syndrome: documented by Thrombolysis in Myocardial Infarction (TIMI) frame count method. Am Heart J 2004; 148: 789-94. [CrossRef]
10. Pirat B, Bozbaş H, Şimşek V, Yıldırır A, Sade LE, Gürsoy Y, et al. Impaired coronary flow reserve in patients with metabolic syndrome. Atherosclerosis 2008; 201: 112-6. [CrossRef]
11. Perticone F, Ceravolo R, Candigliota M, Ventura G, Iacopino S, Sinopoli F, et al. Obesity and body fat distribution induce endothelial dysfunction by oxidative stress: protective effect of vitamin C. Diabetes 2001; 50: 159-65. [CrossRef]
12. Chen H, Montagnani M, Funahashi T, Shimomura I, Quon MJ. Adiponectin stimulates production of nitric oxide in vascular endothelial cells. J Biol Chem 2003; 278: 45021-6. [CrossRef]
13. Malavazos AE, Ermetici F, Coman C, Corsi MM, Morricone L, Ambrosi B. Influence of epicardial adipose tissue and adipocytokine levels on cardiac abnormalities in visceral obesity. Int J Cardiol 2007; 121: 132-4. [CrossRef]
14. Teragawa H, Mitsuba N, Nishioka K, Ueda K, Kono S, Higashi Y, et al. Impaired coronary microvascular endothelial function in men with metabolic syndrome. World J Cardiol 2010; 7: 205-10. [CrossRef]
15. Tok D, Özcan F, Kadife İ, Turak O, Cağlı K, Başar N, et al. Impaired coronary flow reserve evaluated by using echocardiography is associated with increased aortic stiffness in patients with metabolic syndrome: an observational study. Anadolu Kardiyol Derg 2013; 13: 227-34.
16. Mitchell GF, Vita JA, Larson MG, Parise H, Keyes MJ, Warner E, et al. Cross-sectional relations of peripheral microvascular function, cardiovascular disease risk factors, and aortic stiffness: the Framingham Heart Study. Circulation 2005; 112: 3722-8. [CrossRef]