Metabolic Syndrome and Cardiovascular Diseases in Korea

Sunghwan Suh¹ and Moon-Kyu Lee²

¹Division of Endocrinology and Metabolism, Department of Internal Medicine, Dong-A University Medical Center, Busan, Republic of Korea
²Division of Endocrinology and Metabolism, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

There has been a rapid increase in the prevalence of obesity, type 2 diabetes and metabolic syndrome (MetS) over the past two to three decades in most Asian countries. According to the Korean National Health and Nutrition Examination Survey (KNHANES), the prevalence of MetS significantly increased from 24.9% to 31.3% between 1998 and 2007. The clinical significance of MetS is based on the increased risk for the development of cardiovascular disease (CVD). We analyzed the 8-year follow-up data of 2,435 healthy subjects and found that MetS was associated with an increased risk of CVD in both men and women (OR: 1.98, 95% CI: 1.30-3.03 in men; OR: 4.04, 95% CI: 1.78-9.14 in women). MetS was significantly associated with the risk for future coronary heart disease (CHD) in men (OR: 3.68; 95% CI: 1.93-7.01) and stroke in women (OR: 3.96; 95% CI: 1.58-9.94). We also analyzed the echocardiographic findings of 1,600 healthy subjects to evaluate the relationship between metabolic syndrome and left ventricular diastolic dysfunction (LVDD). The patients with MetS exhibited significant differences in parameters of cardiac structure and the LV diastolic function compared to that observed in the patients without MetS. MetS was associated with an increased risk of LVDD (OR: 1.67; 95% CI: 1.18-2.37). These results suggest that the presence of MetS is associated with an increased risk for the development of serious CVD and abnormal changes in the LV structure and diastolic function, even before the development of overt CVD.


Key words: Metabolic syndrome, Cardiovascular disease, Korea

Introduction

Metabolic syndrome (MetS) is a condition characterized by a cluster of metabolic disorders, including abdominal obesity, insulin resistance/glucose intolerance, dyslipidemia and hypertension. The concept of this syndrome was introduced by Reaven in 1988 with respect to the clustering of cardiovascular risks. The prevalence of MetS is increasing worldwide. According to data from the National Health and Nutrition Examination Survey (NHANES) III and NHANESs 1999-2006, the age-adjusted prevalence of MetS increased from 29.2% to 34.2% in the U.S. An increasing trend has also been observed in Asian countries, with MetS presenting as one of the main targets of public health intervention in addition to becoming a growing social and economic problem. In this review, we discuss evidence in Korea of an association between MetS and cardiovascular disease (CVD) and evaluate the possible mechanisms involved.

Defining Metabolic Syndrome

During the past decade, there have been various attempts to standardize the definition of MetS as a diagnostic category, with several institutions propos-
ing a variety of criteria.

The new definition of MetS proposed by the International Diabetes Federation (IDF)\(^4\) and revised by the National Cholesterol Education Program (NCEP)\(^5\) has caused confusion because some patients satisfy the revised NCEP but not the IDF criteria. The characteristics of MetS can differ according to ethnicity and socioeconomic differences. In a study of the 1998 Korean NHANES data\(^6\), the IDF criteria were found to be inferior to the revised NCEP criteria in identifying metabolically abnormal but nonobese groups known to be predisposed to type 2 diabetes and CVD. For this reason, when calculating the prevalence of MetS in Korea, the revised NCEP definition is preferred to the IDF definition, and the majority of Korean studies of MetS use the modified criteria.

**Metabolic Syndrome in Korea**

Korea experienced a major economic crisis in 1998, followed by a rapid recovery achieved by adopting Western policies and cultural values. This industrialization and economic growth were accompanied by a so-called ‘westernization’ of the Korean lifestyle, characterized by a high-calorie diet, obesity and physical inactivity that has brought about negative health consequences. As a result, the age-adjusted prevalence of MetS in Korea increased rapidly from 24.9% in 1998 to 31.3% in 2007\(^7\). Among the five components of MetS, the levels of low HDL cholesterol increased most significantly, by 13.8%, over this 10-year period, followed by abdominal obesity and hypertriglyceridemia, with increases of 8.7% and 4.9%, respectively (Table 1). In addition to the increase in the incidence of MetS, the prevalence of diabetes mellitus and obesity has steadily increased\(^8,9\). Ryu \textit{et al.}\(^10\) found that the prevalence of MetS in Korean adolescents 12 and 13 years of age is 5.5%. As expected, MetS is most common in overweight adolescents, with a prevalence of 22.3%, compared to only 1.6% in normal-weight adolescents. Among other cardiovascular risk factors, a high level of obesity (BMI ≥ 30 kg/m\(^2\)) and a family history of CVD are the strongest independent predictors of MetS based on data obtained from the Korean National Health Insurance Corporation Survey 2008\(^11\).

### Table 1. Changes in the prevalence of each component of metabolic syndrome in Korea

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Metabolic syndrome</td>
<td>24.9</td>
<td>29.2</td>
<td>30.4</td>
<td>31.3</td>
</tr>
<tr>
<td>Abdominal obesity</td>
<td>32.5</td>
<td>34.5</td>
<td>35.3</td>
<td>41.3</td>
</tr>
<tr>
<td>High triglycerides</td>
<td>28.3</td>
<td>33.2</td>
<td>29.9</td>
<td>33.2</td>
</tr>
<tr>
<td>Low HDL</td>
<td>36.4</td>
<td>48.4</td>
<td>51.9</td>
<td>50.2</td>
</tr>
<tr>
<td>High blood pressure</td>
<td>41.0</td>
<td>37.0</td>
<td>37.5</td>
<td>34.5</td>
</tr>
<tr>
<td>High fasting glucose</td>
<td>23.9</td>
<td>25.5</td>
<td>23.3</td>
<td>26.3</td>
</tr>
</tbody>
</table>

The data are presented as percentages. The revised NCEP Adult Treatment Panel III\(^5\) and Asia-Pacific criteria for abdominal obesity (waist circumference > 90 cm in men and > 80 cm in women) were used. KNHANES: Korea National Health and Nutritional Examination Survey.

**Metabolic Syndrome and Cardiovascular Diseases**

It is well documented that MetS is associated with an increased risk of all-cause mortality and CVD\(^12-14\). A meta-analysis conducted by Gami \textit{et al.}\(^15\) that included 36 different prospective studies found that the overall relative risk of CVD among individuals with MetS is 1.78 (95% CI: 1.58-2.00). We also demonstrated in a single-center study (median follow-up of 8.7 years) that MetS is associated with a risk of future CVD in both men and women (OR: 1.98, 95% CI: 1.30-3.03 in men; OR: 4.04, 95% CI: 1.78-9.14 in women)\(^16\). Other Korean studies have also verified a positive relationship between MetS and CVD\(^17-19\), with hazard ratios in the vicinity of 2. These values are close to the estimates obtained in the Asia Pacific Cohort Study Collaboration (APSCS), which gathered individual data for 35 cohorts from the Republic of Korea, China, Hong Kong, Japan, Taiwan, Thailand and Singapore\(^20\). The APSCS data further showed that the more component disorders a patient has, the higher the risk of cardiovascular death. Similarly, the number of MetS components was found to be linearly associated with the risk of a poor outcome in another Korean study\(^19\). Data for 57,237 subjects who attended regular health examinations at a single center in Korea showed that MetS increases the risk of CVD death (RR: 1.75; 95% CI: 1.15-2.66)\(^21\). In addition, the blood pressure component was the key predictor of mortality in that study.
Another study by Hwang et al. found that the fasting glucose level (among all MetS components) has the highest predictive value for CVD in Korean patients with MetS. Recently, Yun et al. reported that MetS is related to the incidence of CVD, independent of insulin resistance (IR). In addition, the combined effects of MetS and IR contribute to increase the risk of CVD. Moreover, one study confirmed a high prevalence of MetS in patients with acute ST-elevation myocardial infarction (STEMI) and found MetS to be an important predictor of in-hospital death among STEMI patients. Kwon et al. also found that MetS is significantly associated with silent brain infarctions in healthy people (OR: 2.83; 95% CI: 1.38-5.82). In a recent article that employed 64-Detector Row Cardiac CT, MetS was found to be strongly associated with significant coronary artery stenosis, multivessel involvement and mixed plaque formation. These results are in line with the findings of other reports showing that MetS is associated with an increased severity of ischemic coronary heart disease (CHD) and that having higher numbers of MetS components is correlated with an increased incidence of CHD and worse CHD outcomes on coronary angiography. The clinical features and cardiovascular risk factors associated with MetS are largely related to the dysregulation of adipose tissue. The adipocytokines secreted by abdominal fat in particular are mediators of inflammation, oxidative stress, insulin resistance and lipoprotein metabolism. These cytokines supervise a subclinical proinflammatory and oxidative state that is thought to accelerate atherosclerosis, plaque rupture and atherothrombosis. In addition, a growing body of evidence now links insulin-like growth factor (IGF) to the development of MetS and increased cardiovascular risks. However, MetS also increases the likelihood of CVD to a greater extent than any of its individual components.

Metabolic Syndrome and the Cardiac Function

As shown above, MetS is characterized by the clustering of cardiovascular risk factors and is associated with the development of CVD and increased mortality. Recently, it has been reported that MetS is associated with an abnormal LV structure and function. Therefore, we investigated a total of 1,599 subjects who underwent medical health checkups at two institutions to determine the association between left ventricular diastolic dysfunction (LVDD) and/or the LV structure and MetS and/or insulin resistance. The results showed that MetS is independently associated with an increased risk of LVDD (OR: 1.67; 95% CI: 1.18-2.37). In addition, as the HOMA-IR value increased, the levels of parameters reflecting the cardiac structure and LVDD significantly increased and the E/A ratio significantly decreased. Furthermore, the LV mass, E/A ratio and E/e' ratio were significantly different across the HOMA-IR quartiles, even after adjusting for other confounders. In accordance with the findings of previous studies, although blood pressure was found to be partly responsible for the development of LVDD in the MetS patients, MetS itself still functions as a risk factor for the development of LVDD, even after adjusting for blood pressure. A rural community cohort study conducted in Korea also found that the degree of MetS clustering is strongly correlated with geometric eccentricity of LV hypertrophy, diastolic dysfunction and arterial changes, irrespective of the patient's age and blood pressure status. The precise pathophysiologic mechanisms underlying the development of this cardiomyopathy are not fully understood. Several factors, including hyperglycemia, hyperinsulinemia, hypertension and increased oxidative stress, have been suggested to explain these structural and functional changes.

Conclusion

In conclusion, the prevalence of MetS is rapidly increasing in Korea. It is clear that MetS is a strong risk factor for the development and increased severity of CVD and confers a greater risk than the sum of its individual components. Moreover, MetS is associated with an abnormal LV structure and function. Considering the social and economic impact of MetS, a national strategy to slow the dramatic increase in the prevalence of MetS should be developed. The first priority should be to reduce the burden of dyslipidemia and abdominal obesity. Lifestyle changes, such as weight reduction, regular exercise and healthy dietary habits, including the consumption of low amounts of sodium, carbohydrates and fat, should be emphasized in order to reverse this deterioration.

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Conflicts of Interest

None.

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