Factors Associated With Metabolic Syndrome That Affect Prognosis in Heart Failure Patients

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Heart failure (HF) is not a disease involving a single organ, but is a progressive systemic chronic disease. Although various medicines and methods for treating HF have been developed in recent years, prognosis in the case of severe HF remains poor.

There have been a large number of publications on prognosis in HF. According to the Framingham heart study conducted in a general population of Western countries, of 5,143 cases that were followed for 14.1 years on average, HF developed in 392 cases, and hypertension preceded in 91% of these cases. As compared with subjects having normal blood pressure, the risk of hypertensive subjects developing congestive HF was 2- and 3-fold greater for men and women, respectively, and the reported survival periods after developing hypertensive HF were short; namely, 5-year survival rates were 24% and 31% for men and women, respectively. The JCARE-CARD study, which is a registration study of chronic HF in Japan, followed the registered cases for 2.4 years on average and reported an annual mortality rate of approximately 9% and an annual rehospitalization rate for HF of approximately 23%. In addition, the CHART-1 study, which is a cohort study of 1,154 HF patients in the northeastern region of Japan, followed the patients for 1.9 years on average and reported an annual mortality rate of approximately 7% and an annual rehospitalization rate for HF of approximately 18%.

Factors affecting prognosis in HF have been reported by the EPESE (Established Population for Epidemiologic Studies of the Elderly program). In that prospective study of 1,749 cases in an elderly population, HF developed in 173 cases.

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Figure. Relationships between factors associated with metabolic syndrome and heart failure.
reported risk factors for HF included (1) sex (male), (2) advanced age, (3) diabetes, (4) pulse pressure $\geq 70$ mmHg, and (5) BMI $\geq 28$ kg/m$^2$. In a study of HF patients conducted in the north-eastern region of Japan, multivariate Cox regression analysis indicated that age ($\geq 70$ years), diabetes, and decreased left ventricular function were significant factors, and similar risk factors as in Western countries have also been reported in Japan. In addition, as factors for inferring prognosis, it was reported that newly developed atrial fibrillation and subclinical microalbuminuria increase the risk of death and heart trouble in HF patients.

In recent years, metabolic syndrome (MetS) has been attracting attention, and there are similarities between the risk factors for HF reported in EPESE and the diagnostic criteria for MetS. MetS is a pathological condition in which arteriosclerotic diseases, such as visceral obesity, insulin resistance (hyperglycemia), dyslipidemia (hypertriglyceridemia, hypo-high density lipoproteinemia), and increased blood pressure, and risk factors for developing type 2 diabetes develop in an individual. Visceral fat accumulation is a cause of MetS, and abdominal circumference has been used as an indicator. As compared with subjects who are not afflicted with MetS, affected subjects have been reported to have a $3$- to $6$-fold greater risk of developing type 2 diabetes and a $1.5$- to $2$-fold greater risk of developing vascular diseases and suffering cardiovascular death.

In this issue of the Journal, Tadaki et al. report interesting results of their analyses from a large-scale clinical trial conducted in Japan with regard to the effects of MetS on HF patients (Figure). First, MetS is a factor that affects prognosis in Japanese HF patients in the case of men, but not in the case of women. Second, of the diagnostic criteria for MetS, abdominal circumference and diabetes are factors that affect prognosis. Furthermore, this report examines individual diagnostic criteria established by various countries and academic societies for MetS and its prognosis in HF patients, and indicates that the diagnostic criteria being used in Japan and Asia for MetS are appropriate for indicating prognosis in HF patients.

Although various organizations and countries have published diagnostic criteria for MetS, in the criteria of the International Diabetes Federation (IDF) and those jointly established by 8 Japanese academic societies (Japanese criteria), visceral fat accumulation is considered to play a major role, and an increase in the abdominal circumference is included as a required item from the viewpoint of it being a simple method of screening subjects in their work places for high-risk of MetS. Insulin resistance is considered to be a major pathological condition of MetS in the criteria of the World Health Organization (WHO). On the other hand, the criteria of the National Cholesterol Education Program (NCEP) and those of the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI), which are revised NCEP criteria, do not have a required item for MetS diagnosis from the viewpoint that it is unclear whether there is a single cause of MetS.

More recently, the IDF, NHLBI, AHA, WHO, the International Atherosclerosis Society, and the International Association for the Study of Obesity jointly established unified diagnostic criteria for MetS, which were published in 2009.

Although the included items for diagnosing MetS are the same as in the previously published criteria, the unified criteria are characterized by there being no required items and the different criteria being used for abdominal circumference measurement depending on race.

It has been reported that, even within the same population, different diagnostic criteria produce different results with regard to the frequency of MetS, risk of developing type 2 diabetes, and risk of developing vascular diseases, including HF, and thus a future task to be addressed includes setting cutoff values for the individual constituent elements.

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