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Stress-Induced Cardiomyopathy: A Need for Prospective Multicenter Trials

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Introduction

Stress-induced cardiomyopathy (also called Takotsubo cardiomyopathy, apical ballooning, or broken heart syndrome) was first reported in 1991 as "myocardial stunning due to simultaneous multivessel coronary spasms: a review of 5 cases" by Japanese doctors,[1] and is well known disease entity now. This disease primarily affects postmenopausal women after psychological or physical stress.[2] Clinical characteristics are a triad of sudden onset of chest pain or dyspnea, electrocardiographic findings with ST segment elevation and evolutional T-wave changes, and a moderate elevation in cardiac enzymes mimicking acute myocardial infarction.[3] As a precaution, coronary angiography is usually performed to differentiate from acute coronary syndrome. Even though many case and clinical study reports have been published, the mechanisms of stress-induced cardiomyopathy (SCM) are still unknown. The pathophysiology of SCM is includes vasospasm of coronary arteries; disturbance of microcirculation; obstruction of the left ventricular outflow obstruction; catecholamine-mediated myocardial stunning, which is an important link between emotional or physical stress and cardiac injury; hormonal interactions; and inflammation.[4-7]

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Clinical Characteristics and Adverse Events

Lee et al.[3] report some different clinical characteristics and prognoses of SCM in this issue.

In their study,[8] they found that in 32 of 39 patients (82%), a major triggering factor is physical stress due to medical illness or procedure, that common presenting symptoms are dyspnea (18/39, 46%) rather than chest pain, and that the prevalence of cardiogenic shock (13/39, 33%) and mortality (3/39, 8%) are very high when compared with the data reported by Gianni et al.[9] However, the data published recently by Song et al.[10] on a study done in Korean subjects is very similar to the data of Lee et al.[3] in clinical characteristics of SCM and the prevalence of cardiogenic shock. Additionally, according to these findings, racial differences may be a factor. The significance of the interpretation of these studies is limited, however, because each has enrolled only a small numbers of patients and been carried out in a single center.

Biomarkers in the Pathophysiology and Clinical Outcomes

A study by Dorfman and Iskandrian[11] shows that serum b-type natriuretic peptide (NT-proBNP) and catecholamine level at presentation correlates with the Killip class of heart failure and associated complications, and low levels predict favorable outcomes. Madhavan et al.[12] has suggested that marked systemic inflammatory response occurs in SCM, similar to those seen in acute myocardial infarction, despite the absence of significant myocardial injury. Morel et al.[7] recently published a study that shows that elevated C-reactive protein (CRP) levels were correlated with baseline left ventricular ejection fraction (LVEF) and BNP levels, and that inflammatory status in SCM was related to LVEF impairment and to the extent of neurohormonal activation. Lee et al.[3] reported

similar findings, showing that elevated high-sensitivity CRP (hs-CRP) and decreased left ventricular systolic function at admission were related to death or cardiogenic shock.

Hence, as described above, various biomarkers and clinical parameters may act as prognostic and pathophysiological markers for SCM, but causal relationships are as yet unkown. Hs-CRP is non-specific inflammatory marker, and many cases of SCM are triggered by physical stress such as a medical illness or surgical procedure. High levels of hs-CRP can be due to severity of the associated disease. Therefore, cases with cardiogenic shock or mortality should be reviewed for the severity of the associated underlying disease. Also, in the study reported by Lee et al.[3] patients reported to have had cardiogenic shock should be reviewed and possible re-classified because the criteria for shock herein included all types of shock and the prevalence of cardiogenic shock is thus very high in this study when compared with data from other studies showing favorable prognoses.

In conclusion, a prospective, multicenter, large volume clinical study of SCM is needed. We have had many case reports and small, single-center study results and now know pathophysiology and clinical importance of SCM very well. Along with ongoing basic research on the cardiac reaction to psychological and physical stress, a multicenter clinical trial would potentially show a straightforward correlation between the pathophysiology and clinical outcomes of SCM, and direct clinicians toward specific treatments.

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