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Variable Morphology of Stress-Induced Cardiomyopathy

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Since the first report by Dote et al.,[1] stress-induced cardiomyopathy (SCMP) also called Takotsubo cardiomyopathy, transient left ventricular apical ballooning, or broken heart syndrome, has been increasingly recognized. SCMP is characterized by transient mid- and apical-segment left ventricular dysfunction in the absence of significant angiographic coronary stenosis, and it primarily affects postmenopausal women after psychological or physical stress. Clinically, SCMP is characterized by a combination of sudden-onset chest pain or dyspnea, an abnormal electrocardiogram (ECG) with ST-segment elevation and T-wave changes, and positive cardiac biomarkers mimicking acute myocardial infarction.[2] Therefore, SCMP should be considered in the differential diagnosis of acute myocardial infarction. Over the years, the criteria for the diagnosis of SCMP have evolved and the recent criteria were proposed by the Mayo Clinic in 2008.[3]

Recently, the reverse or inverted morphological pattern as a variant of this disease has been recognized, with involvement of the basal- and mid-ventricular segments and normal contractility of the apical segments.[4-6] However, data on the clinical characteristics, laboratory findings, echocardiographic parameters and in-hospital outcome of this variant are limited compared to typical SCMP.[7-10]

In their article in this issue of the *Journal of Cardiovascular Ultrasound* titled "Different characteristics between patients with apical and non-apical subtypes of stress-induced cardiomyopathy", Lee et al.[11] reported that the type of preceding stressor and clinical presentation, including chest pain, pulmonary edema, cardiogenic shock, and in-hospital mortality, are similar, the exception being hypertension. However, patients with the non-apical type are younger than patients with the apical type, and the latter have a higher regional wall-motion abnormality (RWMA) index, more frequent T-wave inversion, and longer QT interval and corrected QT interval. This result is similar to reported data on age and ECG findings (Table 1).

Regarding the clinical presentation, however, Hahn et al.[7] and Song et al.[9] reported that fewer patients with the non-apical type developed cardiogenic shock and pulmonary edema. Additionally, unlike Lee et al.,[11] Ramaraj and Movahed[8] and Song et al.[9] reported that the non-apical type is always triggered by emotional and physical stress. Regarding cardiac enzymes, only Song et al.[9] reported that a higher creatine kinase MB fraction and troponin-I in the non-apical type. They explained that the non-apical type had the greater extent of affected myocardium.

Lee et al.[11] reported no deaths, unlike previous studies. Although the long-term prognosis for SCMP is relatively good, recent studies have suggested that the short-term prognosis is not as favorable as generally considered.[7][10][12][13] Furthermore, underlying conditions, old age, hemodynamic compromise, lower left ventricular systolic function, acute physiology and chronic health evaluation II score and high-sensitive C-reactive protein are associated with the prognosis.[10][12][14] Therefore, it is important to interpret the results of these studies carefully because they enrolled only small numbers of patients in a single centers except the study of the Kwon et al.[10]

The clinical features of non-apical ballooning are similar to those of typical apical ballooning and suggest a common pathophysiological etiology. Several mechanisms have been proposed to explain SCMP, but its pathophysiology is not clear. Catecholamines may play a role in triggering SCMP because patients often have preceding emotional or physical stress. In clinical studies, mental stress has been demonstrated to reduce the left ventricular ejection fraction and, rarely, induce RWMA in conjunction with a rise in catecholamines.[15] Wittstein et al.[16] reported increased levels of catecholamines and their metabolites at the time of presentation that remained elevated for 7-9 days. In a study of eight patients with SCMP, myocardial scintigraphy with ^{123}I-metaiodobenzylguanidine showed evi-

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Table 1. Comparison of characteristics between apical vs. non-apical SCMP in several studies

	Number	Classification (n)	Age, yr	Female gender	Preceding stress (%)	Frequency of T wave inversion	Peak troponin I, ng/m	LVEF, %
Hahn et al.[7]	47	Apical (31) vs. nonapical (16)	70 vs. 58*,†	26 (84) vs. 11 (69)	22 (71) vs. 15 (94)	30 (97) vs. 11 (69)*	4 vs. 4†	-
Ramaraj and Movahed[8]	60	Other type (46) vs. reverse (14)	62 vs. 36*	42 (91) vs. 12 (86)	39 (85) vs. 14 (100)*	-	4.2 vs. 5.3	-
Song et al.[9]	103	Other type (83) vs. reverse (20)	64.0 vs. 54.5*,†	60 (72) vs. 10 (50)	64 (77) vs. 20 (100)*	67 (81) vs. 12 (60)*	1.6 vs. 13.1*,†	41.3 vs. 37.7
Kwon et al.[10]	208	Apical (140) vs. nonapical (68)	68.7 vs. 59.8*	101 (72) vs. 50 (74)	121 (86) vs. 65 (96)	93 (66) vs. 35 (52)*	1.23 vs. 1.26	40.9 vs. 40.9
Lee et al.[11]	56	Apical (49) vs. nonapical (7)	73 vs. 52*	40 (82) vs. 4 (57)	41 (94) vs. 6 (86)	46 (96) vs. 4 (57)*	2.74 vs. 1.81	43.6 vs. 46.7

*Statistically significant, †Presented as median. SCMP: stress-induced cardiomyopathy, LVEF: left ventricular ejection fraction

dence of cardiac sympathetic hyperactivity, which improved after 3 months.[17] Nevertheless, the apical preponderance of ballooning is not understood. Recently, Lyon et al.[18] proposed that β2 adrenoreceptors, which protect cells against the pro-apoptotic effects of intense β1 adrenoreceptor activation in the presence of high circuating catecholamine levels, are negatively inotropic and relatively abundant at the apical myocardium, thereby stunning the apical myocardium. However, the apex may not be more vulnerable to catecholamine excess than the mid-ventricle or base in all patients. In other words, individual variation in regional myocardial vulnerability may determine the location of the RWMA. Based on their finding that that patients with non-apical type SCMP are younger than those with apical type SCMP, Ramaraj and Movahed[8] hypothesized that the presentation of inverted SCMP at a young age may be due to the abundance of adrenoceptors at the base compared to the apex. This finding is compatible with other studies[7][9][10] and suggests that differences in the location or amount of adrenoceptors with aging affect the different ballooning patterns of SCMP. However, further studies are needed to clarify the underlying pathophysiological mechanisms of SCMP.

In conclusion, heightened awareness of SCMP has led to more reports and the discovery of variants of SCMP, including mid- or basal left ventricular wall motion abnormalities. However, the literature is based mainly on case reports and small, single-center studies. Moreover, the pathophysiological mechanism of SCMP is poorly understood. Therefore, a prospective, multicenter, large-volume clinical study including catecholamine measurements, magnetic resonance imaging, viral antibody titers, and pathology is needed to define its pathophysiology, prognosis, and specific treatment.

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