Takotsubo Cardiomyopathy and Left Ventricular Outflow Tract Obstruction
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Takotsubo cardiomyopathy often occurs in elderly women after emotional or physical stress. Such stresses cause catecholamine excess that has myocardial toxicity through direct myocardial cell injury, epicardial coronary artery spasm, microcirculation dysfunction, and enhanced inflammation. The apical myocardium is more responsive to sympathetic stimulation, which may make it more vulnerable to catecholamine surge. Catecholamine excess, originating from circulating systemic sources or from cardiac sympathetic nerves, seems to play an important role in the pathogenesis of takotsubo cardiomyopathy. In addition to catecholamine excess, several hypotheses have been postulated to explain the development of takotsubo cardiomyopathy. However, the underlying patho-mechanisms of takotsubo cardiomyopathy remain unclear.

In 1990, Sato et al first reported 3 Japanese cases characterized by chest pain, electrocardiographic changes and reversible left ventricular (LV) systolic dysfunction with apical ballooning mimicking acute myocardial infarction (AMI) but in the absence of epicardial coronary artery obstruction (Figure 1). It was given the name of takotsubo cardiomyopathy because of its unique systolic LV morphology resembling a Japanese octopus trapping pot (a tako-tsubo). Since then, numerous similar cases have been described in Japan and from other countries. Takotsubo cardiomyopathy is now recognized as an established clinical entity.

Figure 1. The first case of takotsubo cardiomyopathy. On September 29, 1983, a 63-year-old woman complained chest pain and was admitted to Hiroshima City Hospital. Electrocardiography showed ST-segment elevation in precordial leads (Left). Under the diagnosis of suspected acute myocardial infarction, emergency cardiac catheterization was performed. Left ventriculography revealed “takotsubo-like” left ventricular wall motion abnormality (Middle). Coronary angiography found no stenosis in epicardial coronary arteries (Right).
It has been generally considered that takotsubo cardiomyopathy is a benign cardiac condition. In most cases, the clinical course is favorable and LV dysfunction spontaneously disappears in a few weeks. However, in some cases, serious complications, including cardiogenic shock, may occur. Although their clinical presentation resembles AMI, it is a unique feature of takotsubo cardiomyopathy that cardiogenic shock may be accompanied by LV outflow tract (LVOT) obstruction. Detection of LVOT obstruction is clinically very important, because the use of inotropic agents may deteriorate the hemodynamic instability by increasing the LVOT pressure gradient.

LVOT obstruction increases apical LV wall stress and LV filling pressure. Increased oxygen demand and reduced coronary perfusion may produce apical myocardial ischemia, regional wall motion abnormality and stunning. Merli et al reported 4 cases of takotsubo cardiomyopathy complicated by LVOT obstruction. After normalization of LV wall motion with no residual LVOT pressure gradient, the patients underwent low-dose dobutamine stress echocardiography that provoked the LVOT pressure gradient. During dobutamine stress, transient wall motion abnormality of the apical myocardial segment was reproduced. Merli et al hypothesized that this increased wall stress in the apical chamber in conjunction with catecholamine excess induced widespread subendocardial ischemia and takotsubo-like LV wall abnormality. However, it is unlikely that LVOT obstruction is the cause of takotsubo cardiomyopathy because most of these patients do not have LVOT obstruction. Takotsubo cardiomyopathy is characterized not only by reduced apical LV wall motion but also hyperkinesis of the basal LV wall. This combination causes the LVOT obstruction in takotsubo cardiomyopathy. LVOT obstruction is not a prerequisite but does play a contributory part in a deteriorating clinical course of takotsubo cardiomyopathy.

In this issue of the Journal, Kawaji et al report on their investigation of the prevalence, clinical presentation and outcomes of takotsubo cardiomyopathy complicated by LVOT obstruction. Previous studies have reported a prevalence of LVOT obstruction ranging from 19% to 25%, but Kawaji et al detected LVOT obstruction in 33% of patients with takotsubo cardiomyopathy. These data indicate that a considerable number of patients with takotsubo cardiomyopathy have LVOT obstruction. Although there was no significant difference in the demographic variables and LV ejection fraction, patients with LVOT obstruction were more likely to suffer from cardiogenic shock and congestive heart failure. They also had a higher incidence of mitral regurgitation. Patients with LVOT obstruction show systolic anterior motion of the anterior mitral valve leaflet, resulting in high-grade mitral regurgitation. Although there is no consensus on the management of takotsubo cardiomyopathy, LVOT obstruction should be managed similarly to hypertrophic cardiomyopathy. For patients with takotsubo cardiomyopathy complicated by cardiogenic shock, the first step in management is fluid infusion (Figure 2). Urgent echocardiography should be performed to exclude the presence of LVOT obstruction, and then inotropic agents should be administrated. If LVOT obstruction is detected, inotropic agents should not be given and if already started, should be stopped. Previous studies have shown that intravenous β-blockers are useful for treating LVOT obstruction in patients with takotsubo cardiomyopathy. β-blockers restrain the basal LV hyperkinesis, resulting in a reduced LVOT pressure gradient, increased systolic arterial pressure and downgrading of mitral regurgitation. Mechanical support should be considered for refractory cardiogenic shock. Intra-aortic balloon pumping (IABP) is beneficial in most cases, but caution should be taken because afterload reduction by IABP may further deteriorate the LVOT obstruction. In such cases, percutaneous cardiopulmonary support is effective.

Despite a higher incidence of cardiogenic shock, the outcome for patients with LVOT obstruction is favorable, if they are adequately managed. Kawaji et al reported no cardiac deaths during a 3-year follow-up. Recent studies have shown that recurrence of takotsubo cardiomyopathy is not uncommon. As reported in those previous studies, β-blockers could not...
prevent recurrence of takotsubo cardiomyopathy. Further accumulation of experience to clarify its pathophysiology is warrant to establish the optimal management of takotsubo cardiomyopathy.

References