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What Truly Causes the Adverse Outcome in Tako-Tsubo Cardiomyopathy?

Tako-tsubo cardiomyopathy (TTC) can mimic acute myocardial infarction (AMI) and induce pump failure and hemodynamic instability. Misdiagnosing TTC as AMI might misdirect the therapy and cause further hemodynamic crisis. We read the paper by Citro et al. (1) in the February issue of *JACC* (1), who studied the echocardiographic correlates of acute heart failure/shock in TTC. Although significant mitral regurgitation (MR) was considered to have a prognostic implication, their results also raise the following question: with the real-time hemodynamic information provided by echocardiography, are we able to further explore the puzzling pathophysiology underlying TTC, beyond just MR, to guide the effective therapy for acute heart failure/shock?

Although most TTC patients appear to have poorer systolic function than that in AMI patients, their left ventricular (LV) filling pressures are paradoxically lower (2). LV outflow tract obstruction (LVOTO) is not commonly reported in stable TTC. However, dynamic LVOTO plays a more important role in TTC-associated cardiogenic shock. Low LV diastolic filling pressure, hyperdynamic motion of basilar walls, pre-existing basal septal hypertrophy and systolic anterior motion (SAM) of the anterior leaflet of the mitral valve, and inappropriate catecholamine treatment could all cause dynamic LVOTO (Fig. 1). LVOTO and SAM usually disrupt coaptation of mitral valve and worsen MR, which further decreases cardiac output (Fig. 1).

The characteristic hyperkinetic right ventricular (RV) function in TTC patients with cardiogenic shock might also reflect an adaptive physiological response to the low LV preload/low cardiac output (3). In contrast to hyperkinetic motion of RV free wall, RV apex tethers to an akinetic LV apex and appears hypokinetic (reverse McConnell’s sign [Online Videos 1 and 2]). In these patients, hyperkinetic RV contractility increases the gradient between the right ventricle and right atrium. Meanwhile, MR increases the pulmonary venous pressure and RV afterload. Both mechanisms result in a dynamic increase in regurgitant volume of tricuspid regurgitation, despite unchanged tricuspid regurgitant orifice area. Increased tricuspid regurgitation worsens RV failure and hemodynamics (4).

Recently, basic research (5) suggests that TTC is mediated by the epinephrine signaling transduction pathway, which has evolved to be a cardioprotective strategy. Clinical evidence supports this self-protective role. Acute LV dilation in TTC lowers filling pressure, not only protecting the vulnerable myocardium within the left ventricle from injury, but also avoiding abrupt pulmonary edema. The less vulnerable myocardium, the RV, and basilar LV walls, remain a functional conduit and detours blood flow directly toward the LVOT to maintain cardiac output until the excessive catecholamine surge subsides. Acute heart failure/shock will not occur unless significant structural or hemodynamic abnormalities interrupt this otherwise harmonic machinery. Thus, uncovering the unique pathophysiology underlying heart failure/shock in TTC can help the effective therapy. Maintaining good LV preload and reducing dynamic LVOTO and the severity of MR/TR should be the main therapeutic targets in the acute phase of TTC. Unnecessary invasive procedures and harmful pharmacological treatment will become the real cause of adverse sequelae.

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APPENDIX For supplemental videos, please see the online version of this article.

REPLY: What Truly Causes the Adverse Outcome in Tako-Tsubo Cardiomyopathy?

We thank Drs. Liu and Krone for their comments and the elegant reconstruction of the pathophysiology of tako-tsubo cardiomyopathy (TTC). Echocardiography allows rapid bedside assessment of cardiac function and provides, beyond the evaluation of left ventricular (LV) function, distinctive findings such as LV outflow tract obstruction (LVOTO), reversible significant (moderate/severe) mitral regurgitation (MR), and right ventricular (RV) involvement that are associated with acute hemodynamic deterioration and poor outcome in TTC(1–3). The degree of reversible LVOTO is variable, depends on loading conditions, and may be associated with systolic anterior motion of the mitral valve (SAM), often leading to significant MR. In our study, the prevalence of LVOTO was 12.8%, and coexistence of LVOTO and SAM was documented in 34.7% of patients with major complications (3). In this patient subset, inotropic agents causing enhanced basal contractility and diuretic agents inducing volume depletion may increase the intraventricular pressure gradient with subsequent hemodynamic instability, ultimately leading to cardiogenic shock. Thus, in patients with cardiogenic shock, the use of intra-aortic counterpulsation is recommended, and inotropic agents and excessive dehydration should be avoided.

FIGURE 1 Dynamic LVOT Obstruction and MR in TTC Patients With Heart Failure/Shock

(A1, B1, D1, E1) Acute myocardial infarction (AMI). (A2, B2, C2, D2, E2): Tako-tsubo cardiomyopathy (TTC) (Online Videos 1 and 2). (A1, A2) Color Doppler studies show turbulent flow in left ventricular outflow tract (LVOT) in tako-tsubo cardiomyopathy (TTC), but not in AMI (yellow arrows). (B1, B2) Pulsed-wave Doppler studies show decreased ejection time in TTC compared with that in AMI (green arrows). (C1, C2) Continuous-wave Doppler studies show increased gradient across LVOT in TTC compared with that in AMI (green arrows). (D1, D2) Color Doppler studies show central mitral regurgitation (MR) jet in AMI and anteriorly directed MR jet in TTC (yellow arrows). (E1, E2) Continuous wave Doppler studies show pan-systolic MR in AMI and late-systolic MR in TTC (green arrows). LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle.