$$\text{ORRI} = \frac{\text{baseline life}}{\text{shortest plaque life among all crack initializations}}$$

and the acute rupture risk index (ARRI) was defined as maximum of the rupture risk index among all cracks ruptured at the pool, that is:

$$\text{ARRI} = \frac{\text{baseline life}}{\text{shortest plaque life among all acute ruptures}}$$

The Young's modulus of the arterial wall, the fibrous cap, and the lipid pool was chosen as 0.3, 0.6, and 0.02 Mpa, respectively. Poisson's ratio for all components was set equally as 0.48. The fatigue parameters c and m were chosen as 1 and 2.6. **Figure 1B** shows the finite element modeling process for 1 case.

The ARRI values in plaques of symptomatic patients were significantly higher than those of asymptomatic patients (44.2 ± 62.6 vs. 10.6 ± 17.7, $p = 0.003$). No difference was found for the ORRI value ($p = 0.61$). It is interesting to find an obvious difference of the ORRI rupture path between the symptomatic and asymptomatic patients. In the symptomatic group, 78% (14 of 18) of the ORRI rupture path was toward the lipid pool; in contrast, there were only 12% (2 of 16) for the asymptomatic group. It seems that the cross-sectional geometry of an asymptomatic patient may successfully avoid an acute pool-rupture event. **Figure 1C** shows RRI results for 1 symptomatic patient and 1 asymptomatic patient.

The risk index defined here is a composite factor, which comprises vessel cross-sectional geometry, material property, blood pressure, heart rate, and so on. It is also an overall value on the whole rupture path, so that local high stress may not significantly affect it. This finding may indicate that fatigue crack growth under pulsatile pressure is a mechanism for atheromatous plaque rupture. Thus, the fatigue model may be a useful tool to predict and assess plaque vulnerability, if further validated by large-scale longitudinal studies.

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Complexity of Assessment and Management of Tako-Tsubo Cardiomyopathy

We greatly enjoyed reading the paper by Citro et al. (1), entitled "Echocardiographic Correlates of Acute Heart Failure, Cardiogenic Shock, and In-Hospital Mortality in Tako-Tsubo Cardiomyopathy," which was recently published in *iJACC*. The investigators (1) sought to determine the clinical and echocardiographic correlates of acute heart failure, cardiogenic shock, and in-hospital mortality in Tako-Tsubo cardiomyopathy (TTC) patients. Although we commend the investigators for their valuable study and the data that they provided, some comments may be beneficial.

In the study, the diagnosis of TTC was on the basis of Mayo Clinic criteria, and the investigators mentioned that performing cardiac magnetic resonance (CMR) was not available in the early evaluation of patients with acute coronary syndrome or similar conditions. In patients with myocardial infarction-like clinical syndromes (e.g., myocarditis, coronary vasospasm, and TTC), further evaluation should be planned to detect etiology and manage specific treatment. When the etiology remains unclear and needs to be determined precisely, CMR appears to be a useful imaging modality for establishing the diagnosis and differentiating it from the etiology of cardiac wall motion abnormalities (2). Infarct-like clinical syndromes are characteristic in late gadolinium enhancement (LGE) patterns (2,3). No or minimal LGE on CMR imaging is characteristic in TTC, and mid-myocardial LGE is characteristic in myocarditis, whereas subendocardial LGE is characteristic in myocardial infarction (2,3). Establishing the exact etiology of cardiac wall motion abnormalities will help in management, thereby avoiding harmful medications and interventions.

The investigators also mentioned that in patients with left ventricular (LV) outflow tract obstruction (LVOTO) and markedly impaired LV systolic function, beta-blockade and intra-aortic balloon counterpulsation should be the preferred treatment options,

compared with inotropic agents, to prevent the development of significant intraventricular gradients and subsequent hemodynamic deterioration. A word of caution should be added—in patients with cardiogenic shock associated with LVOTO, inotropic agents, vasodilators, and diuretic agents, as well as intra-aortic balloon counterpulsation may lead to worsening of shock and worse outcomes (4-6). Balloon deflation further accelerates the blood flow across the LVOT, thereby increasing systolic negative pressure in the aorta and LVOT pressure gradients (5,6).

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REPLY: Complexity of Assessment and Management of Tako-Tsubo Cardiomyopathy

We are grateful to Drs. Yalcinkaya and Celik for their interest in the results of our study (1). The diagnosis of Tako-Tsubo cardiomyopathy (TTC) is sometimes challenging, and a detailed knowledge of this peculiar syndrome is required. Recently, our group proposed a revised form of the current diagnostic criteria for TTC that might increase the likelihood of correctly identifying this entity (2). We acknowledge that an integrated multi-imaging approach seems reasonable in TTC, especially when multiple etiologies at presentation deserve an accurate diagnostic workup. Cardiac magnetic resonance (CMR) imaging provides useful information in differential diagnosis to confirm or rule out TTC. In a large, prospective, multicenter study, TTC was correctly identified by CMR performed at a median of 3 days after hospital admission, but no information was reported as to whether unstable patients were enrolled (1 patient with cardiogenic shock did not undergo CMR) (3). In our opinion, CMR should be considered as an alternative technique to echocardiography, and should not be performed in all patients, but only in some difficult and challenging cases (4). In addition, because of its limited availability, the necessity of leaving the intensive care unit, and the duration of the examination, the diagnostic performance of CMR in unstable patients makes the risk-to-benefit ratio unfavorable. As for treatment of TTC, very few data are available in this field. Obviously, caution is required for the treatment of patients with left ventricular outflow tract obstruction. In this patient subset, beta-blockers and fluids are the first-line treatment options. In our experience, intra-aortic balloon pump should only be used in patients with persistent cardiac shock who do not respond to fluid administration. Generally, inotropic agents should be avoided in these patients, but if the treatment is deemed necessary, we think that norepinephrine rather than epinephrine should be preferred. Veno-arterial extracorporeal membrane oxygenation has been reported as rescue therapy in severe cardiogenic shock refractory to medical treatment and intra-aortic balloon pump in some TTC patients (5). Therefore, therapy should be tailored to different patients' characteristics. Echocardiography is more suitable for bedside monitoring of the dynamic and unique evolution of TTC and should be considered the preferred imaging modality even for therapy guidance.

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