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## THE AUTHORS REPLY:

The letter by Dr. Y-Hassan regarding our editorial (1) on the work by Christensen et al. (2) entitled "Cardiac sympathetic disturbance in Takotsubo cardiomyopathy: primary etiology or a compensatory response to heart failure?" hypothesizes that the local cardiac sympathetic hyperactivation-disruption that occurs in patients with chronic heart failure, regardless of the underlying cause, may in fact be a form of Takotsubo cardiomyopathy occurring in repetitive attacks or in chronic form, triggered by heart failure or its severe symptoms.

In heart failure, the cardiac sympathetic system is activated during left ventricular remodeling, which may mimic the trigger effect of Takotsubo syndrome. However, unlike chronic persistent left ventricular dysfunction in heart failure, Takotsubo cardiomyopathy is a transient left ventricular systolic dysfunction characterized by apical ballooning with relative sparing of the basal segments. Although cardiac sympathetic disturbance has been linked to Takotsubo syndrome as the primary cause in both experimental animals and in human subjects, catecholamine excess may also occur as a consequence of acute myocardial ischemia which can cause myocardial stunning and transient contractile dysfunction. Myocardial stunning triggered by myocardial ischemia from atherosclerotic coronary disease (causing preconditioning and ischemic stunning) or from coronary or microvascular vasospasm in the absence of coronary artery disease (e.g., Takotsubo patients) confer protection against subsequent episodes of ischemia and preserve energy metabolites by downregulating contractile function and metabolism (3). Such repetitive stunning may present clinically as chronic left ventricular dysfunction and heart failure. In repetitive myocardial stunning, a unique metabolic adaptation occurs (abnormal glucose use despite restoration of regional myocardial blood flow) that is different from the adaptation typically described in clinical and experimental models of myocardial hibernation in chronic coronary artery disease (preserved or enhanced glucose use in a region with decreased regional myocardial blood flow) (3).

The Takotsubo patients in the study by Christensen et al. (2) had heart failure with low left ventricular ejection fraction whereas the control subjects consisted of a heterogeneous group of patients with myocarditis or aborted infarction who were not necessarily in heart failure. Moreover, because the $^{123}$I-mIBG scans in the study were performed at the subacute phase of the disease (not before or at the onset of the disease), it is not clear from the data whether cardiac sympathetic disturbance was the primary cause of Takotsubo cardiomyopathy or simply a compensatory response to heart failure (1). Perhaps future studies can provide mechanistic distinction and additional details that may shed light on this intriguing syndrome.

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Please note: The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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## Path to Cardiovascular Multimodality Imaging Subspecialty

I commend the American College of Cardiology Cardiovascular Imaging Council for putting together an excellent document that lays out the landscape of the future of cardiovascular imaging (1). However, as a formally trained multimodality cardiac imager (level III in echocardiography/cardiac magnetic resonance imaging and level II in cardiac computed tomography [CT]/nuclear cardiology) practicing in an academic center, I would like to make several observations. First, the "silos of expertise" approach in cardiac imaging may cause an inherent and, at times, strong bias of referral to certain techniques that might preclude patients from getting more