disruption with deleterious consequences (5). In addition to the ^{123}I-MIBG scintigraphic findings in TS, there is extensive evidence, discussed elsewhere (3), supporting the hypothesis of the presence of a causal link between local cardiac sympathetic hyperactivation-disruption (triggered by emotional or physical stress factors) and TS (3). The local cardiac sympathetic hyperactivation-disruption that occurs in patients with chronic heart failure, regardless of the underlying cause, may also be a form of TS occurring in repetitive attacks or in chronic form triggered by heart failure or its severe symptoms. Cardiac sympathetic hyperactivation-disruption is most probably the primary cause of TS (3), and chronic TS with acute exacerbation may be the main cause of acute deterioration of heart failure in patients with chronic heart failure (5).

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http://dx.doi.org/10.1016/j.jcmg.2016.07.017

Please note: Dr. Y-Hassan has reported that he has no relationships relevant to the contents of this paper to disclose.

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THE AUTHORS REPLY:

The authors greatly appreciate the feedback from Dr. Y-Hassan. In the presented study (1), planar iodine-123-labled MIBG (^{123}I-MIBG) was used to assess late heart-to-mediastinum ratio and ^{123}I-MIBG washout ratio. Because single-photon emission computed tomography imaging was not applied, spatial resolution was not sufficient to assess regional cardiac ^{123}I-MIBG uptake. However, as Dr. Y-Hassan mentions, a regional defect encompassing the akinetic region of the left ventricle is normally present. Plasma epinephrine level fluctuates and varies widely with circadian rhythm, body position, and so forth (2). In the presented study (1), the 95% confidence interval for healthy controls was 17 to 33 pg/ml for epinephrine and 488 to 989 pg/ml for norepinephrine. Of the 32 patients with Takotsubo cardiomyopathy, 4 patients had a normal plasma epinephrine level, ≤33 pg/ml, and 10 patients had a normal plasma norepinephrine level, ≤989 pg/ml. In our study, mean plasma epinephrine levels were approximately doubled in patients with Takotsubo cardiomyopathy compared to those in controls, whereas the study by Wittstein et al. (3) reported tripled levels. The absolute values of plasma epinephrine in our study were not comparable to the striking elevations reported by Wittstein et al. (3), perhaps due to the difference in methods used for catecholamine analysis. As pointed out by Dr. Y-Hassan, it remains unknown whether the observed sympathetic hyperactivity in Takotsubo cardiomyopathy is causal or secondary, but a possible causal link between catecholamine toxicity and Takotsubo cardiomyopathy has been established (4,5).

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http://dx.doi.org/10.1016/j.jcmg.2016.08.017

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

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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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http://dx.doi.org/10.1016/j.jcmg.2016.08.018

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