fluorodeoxyglucose positron emission tomography (2) correctly excluded 2 abscesses.

CTA diagnosed 22 of 25 masses (88%; 13 thrombi/pannus, 8 vegetations, and 1 unclear (ruptured chordae with retracted papillary muscle). Six panni could not be visualized by TEE due to metal reverberation artifacts, although an increased transvalvular pressure gradient was observed. Two panni (n = 1 patient of with 2 bioprosthetic valves) were incorrectly diagnosed by CTA as a "beam hardening artifact" (2 mm) and vegetation (3 mm size), respectively.

Twelve of 12 dehiscences (100%) were correctly diagnosed by CTA. In 4 patients, the full circumferential extent was underestimated by TEE, although "paravalvular leak" was reported.

Sixteen of 17 instances of structural bioprosthetic valve degeneration (94.1%) were detected by CTA, as were 2 of 2 mechanical "stuck valves" (100%) and 3 of 3 abnormalities (100%) after mitral annuloplasty, respectively.

CTA AND TEE VERSUS SURGERY (N = 23)

The accuracy of TEE was c = 0.735 (95% CI: 0.54 to 0.88) and c = 0.912 (95% CI: 0.74 to 0.98; p = 0.003, receiver operating characteristic analysis) for CTA.

In summary, our data show a high accuracy of CTA for detecting PVD, using surgery as the reference standard, particularly for the assessment of paravalvular pathologies (paravalvular leakage, abscess, pseudoaneurysm, or dehiscence) (**Figure 1A**) and identification of thrombi/pannus. CTA further clarified the cause of increased transvalvular pressure gradients (**Figure 1B**, thrombus/pannus) on echocardiography. CTA added value to 2-dimensional TEE for the visualization of the full circumferential extent of dehiscence. In addition, CTA allowed for complementary evaluation of native coronary arteries and bypass grafts.

The study was limited by the absence of 3-dimensional TEE, which should be superior to 2-dimensional TEE for PHV visualization and diagnostic performance.

In conclusion, we advocate TEE as the primary imaging tool for PVD in alignment with the American Heart Association scientific statement (3), with CTA as part of a multimodality diagnostic work-up, with specific recommendations for suspected paravalvular involvement, to characterize pathologies and to fully define the involved anatomic territory; unclear PHV dysfunction on TEE (e.g., increased pressure gradient) without a morphological correlate for thrombus/pannus detection; and PHV mass characterization (thrombus/pannus, vegetation vs. calcification). In view of the high risk of PHV revision surgery, multimodality imaging may be justified in these subgroups.

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^{123}I-MIBG Scintigraphy in the Subacute State of Takotsubo Cardiomyopathy

I read with attention the article by Christensen et al. (1) titled "^{123}I-MIBG scintigraphy in the subacute state of Takotsubo cardiomyopathy." In this article, the authors studied 32 patients with Takotsubo

cardiomyopathy (TTC), using iodine-123-labeled metaiodobenzylguanidine (^{123}I-MIBG) myocardial scintigraphy and measurements of plasma catecholamines to assess adrenergic activity (1). More in detail, these authors showed in subacute follow-up that TTC was associated with a decreased late heart-to-mediastinum ratio (H/Mlate) and increased washout rate (1). The study concluded that adrenergic hyperactivity has a possible role in TTC (1). The adrenergic hyperactivity plays a central role in TTC (2–5). In fact, in a recent study, Marfella et al. (2) reported the elevation of plasma catecholamines (2- to 3-fold times the normal values for epinephrine and <2-fold for norepinephrine), strengthening the hypothesis that TTC patients may be under a "stress condition" as a triggering mechanism of a more complex cardiomyopathy as TTC. In that study, and as supported by Christensen et al. (1), TTC may be triggered by an altered and not balanced sympathetic tone (2). This may be reflected by augmented catecholamine levels and also assessed by ^{123}I-MIBG in a subacute phase of the disease (1). In Marfella's study catecholamine levels was 758 to 1,240 pg/ml, and this value may be variable under different TTC conditions (2). In fact, the authors have described extremely high plasma catecholamine levels and their metabolite elevations (from the index admission day to days 7 to 9), whereas other patients have shown either normal or slight elevation of plasma or urine catecholamines (3,4). It is our opinion that the hyperactivity of sympathetic tone may be a relevant trigger in TTC (2–5) but that TTC may be due to a complex adrenergic tone and adrenergic receptor altered balance (3–5). This investigated aspect looks to be not less relevant than an isolated adrenergic hyperactivity (1–3). It is our opinion that an altered substrate (adrenergic tone, adrenergic transcriptional receptorial, and molecular pathway alterations) localized to specific left ventricle wall portions (as apex) may condition this clinical condition (2–5). Moreover the catecholamine elevation amount (2 to 3 times or more) represents a trigger mechanism, performing its pathological effect through an altered adrenergic receptorial transcription pathways (2,3) and, in particular, ventricle wall segments (2–5). Therefore, these abnormalities may condition the TTC only for a few myocardial wall areas, such as the apex, leading to an apical ballooning (2–5). This remains the crucial discussion point. At the moment, we cannot replace the receptors involved in altered adrenergic signaling in TTC, but we may try to ameliorate sympathetic tone dysfunction by using antioxidative treatments (2). In further studies conducted in TTC animal models, we could study the adrenergic receptorial transcription processes during hyperadrenergic stimulation. Our opinion, in clinical, and instrumental confirmed TTC cases, remains to find the better treatment trying to restore the autonomic system unbalance in these patients (2). The future hope may be to replace the altered adrenergic receptors pathways and to control the adrenergic tone hyperactivity.

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THE AUTHORS REPLY:

We greatly appreciate the feedback from Dr. Sardu and colleagues on our work (1). As mentioned in the letter, adrenergic hyperactivity is assumed to be the underlying cause of Takotsubo cardiomyopathy, and a possible mechanism has been suggested by Lyon et al. (2). Catecholamines may modulate cardiac function indirectly through the coronary vessels (3,4) or through a direct effect on the myocytes (5). Many different mechanisms may thus contribute to the clinical syndrome of acute catecholamine toxicity. The treatment of Takotsubo cardiomyopathy is still purely supportive, but a causal treatment may be accessible in the future.