A fifty-nine year old woman presented to a tertiary care center with a few hours of increasing chest pain suspicious for angina. She reported persistent bouts of nausea and vomiting for 2 days before the onset of chest pain, but denied abdominal pain or hematemesis. She denied any recent physical or emotional stressors. Notably, the patient was congenitally deaf, and all history was obtained through a sign language interpreter. Patient also reported chronic cannabis abuse for many years. Physical examination was remarkable for prominent jugular venous pulsation, bilateral lung crackles, and left ventricular gallop, apart from sensorineural hearing loss. Her ECG showed poor R-wave progression, ST-segment elevation, and T-wave inversion in the precordial leads. An echocardiogram revealed a left ventricular ejection fraction of 20% to 25%, severe hypokinesia of apical and midsegments, and hypercontractile basal segments. Laboratory workup revealed elevated troponin-I (2.1 ng/mL) and creatine kinase myocardial band (16.2 ng/mL). Metabolic panel and blood counts were normal. Urine drug screen was positive for tetrahydrocannabinol. Cardiac catheterization revealed normal epicardial coronaries and left ventricular end-diastolic pressure of 16 mm Hg. Ventriculogram was consistent with apical ballooning, apart from sensorineural hearing loss. Her ECG showed poor R-wave progression, ST-segment elevation, and T-wave inversion in the precordial leads. An echocardiogram revealed a left ventricular ejection fraction of 20% to 25%, severe hypokinesia of apical and midsegments, and hypercontractile basal segments. Laboratory workup revealed elevated troponin-I (2.1 ng/mL) and creatine kinase myocardial band (16.2 ng/mL). Metabolic panel and blood counts were normal. Urine drug screen was positive for tetrahydrocannabinol.

Cardiac catheterization revealed normal epicardial coronaries and left ventricular end-diastolic pressure of 16 mm Hg. Ventriculogram was consistent with apical ballooning, supporting the diagnosis of Takotsubo or stress cardiomyopathy (Figure 1 and Movie I in the online-only Data Supplement). The rest of the course was unremarkable, with no cardiac complications.

Five months later, patient presented to the hospital with another similar episode of hyperemesis syndrome followed by chest pain. She was compliant with medications, including β-blockers and angiotensin-converting enzyme inhibitor, but continued cannabis abuse. Initial echocardiogram at admission was relatively unremarkable, with preserved left ventricular systolic function. A cardiac MRI was done that revealed basal segments hypokinesis (Movie II in the online-only Data Supplement). Echocardiogram repeated the next day revealed obvious basal and midventricular akinesis with hyperdynamic apex (Figure 2 and Movie III in the online-only Data Supplement). The rest of the course was unremarkable, with subsequent improvement of left ventricular systolic function.

Recurrent stress cardiomyopathy with a different pattern of ventricular involvement in the same patient questions the currently proposed hypothesis of variability of β-adrenergic receptor density and sensitivity. Stress cardiomyopathy had been often, but not always, shown to be associated with hypercatecholaminergic states. Although the association between emotional stressors and stress cardiomyopathy is well established, the molecular mechanisms linking cardiac muscles to stress have not been clearly elucidated. Alternative mechanisms linking cardiomyopathy to psychological stresses may be the endocannabinoid system. Endogenously produced cannabis-like substances (endocannabinoids) have recently been shown to have direct (non–receptor-mediated) and cannabinoid receptor type 1 (CB1)–mediated cardiovascular effects. They reduce cardiomyocyte contractility and have been implicated in cirrhotic cardiomyopathy, doxorubicin-induced cardiomyopathy, and sepsis-associated myocardial dysfunction.

Furthermore, CB1 receptor antagonist, rimonabant, was found to be cardioprotective in...
doxorubicin-induced cardiomyopathy. Studies on animal models have suggested a key role for endocannabinoids in the modulation of sympathetic and cardiovascular response during stress. Furthermore, excessive endocannabinoid production states, such as subarachnoid hemorrhage and ischemic stroke, may be implicated as the cause of neurogenic myocardial stunning (which is clinically identical to Takotsubo cardiomyopathy). It is uncertain if exogenous cannabis intake can simulate endocannabinoids or alter endocannabinoid pathways. Cardiovascular adverse events are relatively infrequent with cannabis in comparison with other drugs of abuse like cocaine. Specifically, cardiomyopathy has not been previously reported with cannabis.

We propose that cannabis abuse could be a potential etiology for recurrent left ventricular dysfunction in our patient. Occurrence of both Takotsubo and reverse Takotsubo cardiomyopathy refutes the hypothesis of regional differences in β-receptor sensitivity and density and undermines the role of catecholamines in stress cardiomyopathy. The concurrence of the hyperemesis syndrome with stress cardiomyopathy in our case further supports our argument and suggests cannabis as the common pathogenesis for the 2 processes. Cannabinoid hyperemesis syndrome is a recently described entity observed in habitual marijuana smokers typically presenting as intractable bouts of emesis lasting hours to days after recent excess use. In conclusion, we propose a possible link between cannabis and recurrent stress cardiomyopathy and a potential role of the endocannabinoid system in the pathogenesis of cardiovascular disease, especially stress cardiomyopathy.

Disclosures
None.

References
Recurrent Stress Cardiomyopathy With Variable Regional Involvement: Insights Into Etiopathogenetic Mechanisms
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