Stress-Related Cardiomyopathy Syndromes

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The relationship between the heart and the brain is complex and integral in the maintenance of normal cardiovascular function. Certain pathological conditions can interfere with the normal brain-heart regulatory mechanisms and result in impaired cardiovascular function. The mechanisms through which the central and autonomic nervous systems regulate the heart and the manner in which their impairment adversely affects cardiovascular function have recently been reviewed by Samuels.1 The purpose of this article is to provide an up-to-date review of the clinical presentation of the stress-related cardiomyopathy syndromes, discuss possible causal mechanisms, and highlight the similarities and differences between them.2–16

The stress-related cardiomyopathies appear similar in that they seemingly occur during times of enhanced sympathetic tone and may be precipitated in part or entirely by excessive endogenous or exogenous catecholamine stimulation of the myocardium. Although significant clinical overlap exists in those presenting with stress-associated cardiomyopathy, it is unclear whether myocardial adrenergic hyperstimulation is a unique, reversible cardiomyopathy that appeared to be precipitated by acute emotional stress.2,13,16 They found that these patients were usually postmenopausal women and often developed signs and symptoms of an acute coronary syndrome (ACS) proximate to a strong emotional stressor as associated with a transient apical and midventricular wall motion abnormality despite the lack of obstructive coronary artery disease (CAD) at the time of emergent coronary angiography. This syndrome was initially given the name Takotsubo cardiomyopathy (TC) and has subsequently been referred to as the apical ballooning syndrome and broken heart syndrome. It is now recognized that TC can also occur in the setting of acute medical illness and after surgery. TC has now been reported worldwide and has recently been acknowledged by the American College of Cardiology and American Heart Association as a unique form of reversible cardiomyopathy.17

Clinical Presentation

Those presenting with TC are most commonly postmenopausal women.2–4,18,19 In a systematic review, women accounted for 82% to 100% of patients with an average age of 62 to 75 years, although cases have been described in individuals aged 10 to 91 years.6

The presentation of TC is usually similar to that of an ACS with symptoms primarily consisting of ischemia-like chest pain and ischemia-like ECG changes in most patients. As a result, both US and international guidelines have now included TC as an important differential diagnosis of ACS.20 Collective reports have shown that severe emotional stress has preceded presentation with TC in ~27% of reported cases.19 Reported emotional precipitants have included death of a family member or a pet, public speaking, fierce arguments, financial loss, surprise parties, automobile accidents, and natural disasters such as earthquakes, among others. Nearly one half of the surge in apparent ACS after a major earthquake in Japan in 2004 was actually found to be TC.21 Approximately 38% of TC cases occur in the setting of an acute medical illness or surgery, but, importantly, in some patients no precipitating event can be identified.19

Abnormalities on the ECG are common at the time of presentation, including ST-segment elevation that most often occurs in the precordial leads (Figure 1A).2,4,6 The anterior ST-segment deviation tends to be of lesser magnitude than in patients presenting with anterior ST-segment elevation myocardial infarction (MI) due to documented atherothrombotic occlusion of the left anterior descending coronary artery.22,23 Most series have reported anterior ST elevation at the time of presentation in >90% of TC patients. TC patients stereotypically develop evolutionary deep symmetrical T-wave inversions within 24 to 48 hours after presentation with associated prolongation of the QT interval (Figure 1B), and transient anteroseptal Q waves occur in approximately one third of patients.4 No ECG criteria have been identified that reliably discriminate between TC and ST-segment elevation MI.22 The ECG changes are transient and resolve within months in most cases. A minor elevation in troponin or creatine kinase–MB (CK-MB) at the time of presentation is common.2–14

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However, the magnitude of elevation is disproportionately low given the extent of wall motion abnormality.

Cardiac Catheterization and Angiographic Findings
Despite the clinical presentation, patients with TC typically do not have angiographically identifiable obstructive epicardial CAD that could account for the observed wall motion abnormality (Figure 1C). Several investigators have reported abnormal coronary microcirculatory function at the time of presentation in all 3 epicardial coronary distributions; (2) absence of obstructive epicardial CAD or angiographic evidence of acute plaque rupture that could be responsible for the observed wall motion abnormality; and (3) new ECG abnormalities such as transient ST-segment elevation and/or diffuse T-wave inversions or troponin elevation. Diagnostic criteria are likely to continue to evolve over time as our knowledge of TC improves. Apical-sparing variants have been reported in which the distal apex demonstr-
A meta-analysis found that the most common causes of mortality in TC patients were cardiogenic shock and systemic embolization.32

**Acute and Chronic Management**

No trial data are available to guide clinical management, and therefore treatment decisions are somewhat empiric (Table 3). Sympathetic activation is believed to contribute to the pathogenesis of TC, and thus it is reasonable to consider long-term β-blocker therapy with the goal of preventing recurrence.35 Agents with additional α-adrenergic receptor blocking properties may potentially be superior in this regard. Diuretics should be administered as needed for volume overload. The use of angiotensin-converting enzyme inhibi-

![Figure 1. A, Initial ECG in a 65-year-old woman who presented with TC immediately after an uncomplicated laparoscopic cholecystectomy. She developed chest pain in the recovery room associated with hypotension and ECG changes. The patient had expressed extreme fear of the surgery preoperatively. The ECG shows ST-segment elevation in leads V2 to V6, I, aVL, and II. B, ECG performed 24 hours after symptom onset. This ECG shows the typical evolutionary symmetrical T-wave inversions in the precordial leads. C, Coronary angiogram performed emergently in this patient, demonstrating angiographically normal coronary arteries. RCA indicates right coronary artery. D, End-systolic phase left ventriculogram of the patient demonstrating the typical apical and mid-ventricular wall motion abnormalities characteristic of TC. End-diastolic phase left ventriculogram in the same patient is also shown. Echocardiography 1 month later demonstrated normalization of LV wall motion.](http://circ.ahajournals.org/doi/10.1161/CIRCULATIONAHA.116.026480)
tors or angiotensin receptor blockers should be considered until LV function has normalized. Hypotension after the initiation of an angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, or diuretics has been reported as a result of potentiation of a dynamic LV outflow tract obstruction. Therefore, echocardiography should be performed in patients who develop worsening heart failure or hypotension to assess for the development of an intraventricular pressure gradient. Echocardiography should also be performed before hospital discharge to assess for the recovery of LV systolic function. Surveillance echocardiography should be considered ∼4 to 6 weeks after presentation in those with persistent LV dysfunction at the time of hospital discharge. A short duration of anticoagulation with warfarin may be considered for patients with persistent, significant reduction in LV function to prevent LV thrombus formation and embolization.

Risk of Recurrence
A paucity of data exists on the risk of recurrence after a patient experiences an episode of TC. Most published data suggest that the recurrence rate in the first few years after presentation with TC is likely in the range of 2% to 10%.4,11,36 Theoretically, recurrence rates may be lower in those who are maintained on comprehensive adrenergic blockade if it is assumed that catecholamines play a central role in the pathogenesis of the syndrome.

Mechanisms
The precise pathophysiology of TC is unknown. It has been suggested that transient multivessel epicardial spasm may be responsible,16 although this has been reported in no more than 11% of apparent TC cases in the published literature. Pharmacologically provable multivessel epicardial spasm has been reported in some patients, but its clinical significance remains unclear. Ibanez and colleagues37 have documented the presence of plaque rupture by intravascular ultrasound in the left anterior descending coronary artery of patients with angiographically nonobstructive CAD and a diagnosis of TC. However, this mechanism does not entirely explain the extent of regional wall motion abnormality seen in those without a wraparound left anterior descending coronary artery, the presence of right ventricular dysfunction in some patients, or the preservation of apical function in some patients. Alternatively, others have suggested that a dynamic intraventricular pressure gradient due to midseptal hypertrophy and enhanced catecholamine tone may be the inciting event for TC. Another hypothesis is that of microvascular ischemia in the absence of obstructive epicardial CAD. Multiple reports have documented abnormal myocardial perfusion in the LV apical and midventricular segments that correspond with the regional distribution of the LV wall motion abnormality.6,8,38–40 However, scintigraphic imaging modalities and cardiac magnetic resonance imaging have failed to document myocardial necrosis despite the almost universal finding of mild troponin elevation in TC (Figure 3).11 The precise contribution of

Table 3. Management Considerations in Patients Presenting With Transient Stress-Related Cardiomyopathy

| Monitor in hospital on telemetry; observe for heart failure, arrhythmias, and mechanical complications |
| Perform echocardiogram or magnetic resonance imaging to assess for LV function, mitral regurgitation, LV mural thrombus, right ventricular function, dynamic LV outflow tract obstruction, and other concomitant cardiac conditions |
| Evaluate for dynamic obstruction in the LV outflow tract in those with a new systolic murmur, hypotension, and/or mitral regurgitation |
| Anticoagulation with heparin to prevent LV mural thrombus formation in those with apical involvement if there are no contraindications to anticoagulation; consider oral anticoagulation with warfarin in those with significant persistent LV systolic dysfunction at the time of hospital discharge |
| Standard medical therapy for LV systolic dysfunction including an adrenergic-blocking agent |
| Repeat echocardiography before hospital discharge to reassess LV systolic function; consider repeating echocardiogram at 1 and 3 months in those with persistent LV dysfunction |

Figure 2. Distribution of segmental LV wall motion abnormalities in TC patients assessed with cardiac magnetic resonance imaging. Figure reproduced from Sharkey et al11 with permission from the publisher. Copyright © 2005 the American Heart Association.
myocardial ischemia to LV dysfunction in TC is unclear, and it remains to be established whether impaired myocardial perfusion is a direct cause of the syndrome or an epiphenomenon.

Nuclear imaging techniques utilizing metabolic tracers such as $^{123}$I-$\beta$-methyl-iodophenyl-pentadecanoic acid and $^{18}$fluorodeoxyglucose in acute TC demonstrate significant reduction in regional free fatty acid utilization and extracellular glucose transport, respectively, in the segments with wall motion abnormalities consistent with “metabolic” myocardial stunning (Figure 4).38–40 The cause of this metabolic abnormality is unknown but may be related to myocardial changes associated with catecholamine excess, including intramyocyte calcium overload with associated metabolic derangements, or it could be explained by repeated episodes of ischemia followed by reperfusion.41–45

Catecholamine stimulation is likely to be an important component of the pathophysiology of TC because the syndrome commonly occurs proximate to an acute emotional and/or physical stress. In one study, catecholamine levels and their metabolites were found to be 2- to 3-fold higher in TC patients compared with those presenting with acute MI with a similar degree of clinical heart failure.14 A rat model of TC has been reported in which physical immobilization produces a similar cardiomyopathy that is prevented by pretreatment with an $\alpha$- and $\beta$-adrenergic antagonist (asmulolol).15 Endomyocardial biopsies in some TC patients have demonstrated contraction band necrosis and mononuclear inflammatory infiltrates, a finding consistent with catecholamine-mediated cardiotoxicity. Additionally, reversible intracellular accumulation of glycogen and extracellular accumulation of matrix proteins have been observed, further suggesting an associated myocardial metabolic abnormality.46

The cause of the apparent female predisposition for TC is unknown but may be related to gender differences in myocardial sensitivity to catecholamine toxicity and subsequent intramyocyte calcium overload.47,48 The reason for the unique, noncoronary distribution of wall motion abnormali-
ties in TC is also unknown but may be related to regional differences in myocardial autonomic innervation and to regional differences to myocardial adrenergic stimulation.

**LV Dysfunction Associated With Intracranial Hemorrhage, Ischemic Stroke, and Head Trauma**

Acute LV systolic dysfunction is a well-recognized complication of intracranial bleeding, most commonly occurring after subarachnoid hemorrhage (SAH). Approximately 20% to 30% of patients with SAH manifest a secondary cardiomyopathy and/or regional wall motion abnormality, which is usually reversible in the absence of underlying obstructive CAD. This entity has been referred to as neurocardiogenic stunning and “neurogenic stress cardiomyopathy” (NSC). Independent predictors of NSC after SAH include severity of neurological injury, troponin elevation, CK-MB elevation, elevated brain natriuretic peptide, and female gender. The serum biomarkers of cardiac injury include severity of neurological injury, troponin elevation, CK-MB elevation, elevated brain natriuretic peptide, and female gender. 

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**ECG Changes**

Approximately 75% to 92% of patients with intracranial bleeding or ischemic stroke develop new ECG abnormalities. The most common ECG changes are QT-interval prolongation (45%), ST-segment depression (35%), and U waves (28%). The QT-interval prolongation increases the risk for torsades de pointes and can be accentuated by hypokalemia, which has been observed in up to 50% of those presenting with SAH. QT-interval prolongation is more common with SAH than with other forms of acute cerebrovascular disease and is responsible for the greater relative risk of ventricular tachyarrhythmias with SAH. ST-segment elevation, mimicking acute myocardial injury, can occur in those with acute intracranial pathology, but this finding seems to occur mainly in those with apical and midventricular distribution wall motion abnormalities. As seen with TC, patients with NSC frequently develop evolutionary deep, symmetrical T-wave inversions, the so-called cerebral T-wave. The ECG changes with acute intracranial pathology are thought to result from sympathetically mediated intramyocardial electrolyte disturbances due to myocyte calcium overload and enhanced cellular eflux of potassium ions and subsequent catecholamine-induced myonecrosis.

**Wall Motion Abnormalities**

The most common wall motion abnormality in NSC due to SAH appears to be either hypokinesis of the basal and midventricular segments with sparing of the apex or global LV hypokinesis, whereas the TC pattern is less common. In a recent report of consecutive patients with NSC, 8 of 24 (33%) had isolated apical and midventricular LV hypokinesis with sparing of the basal segments, consistent with TC. Wall motion abnormalities in NSC do not typically correlate with a single coronary artery vascular distribution and are transient, with resolution within days to weeks among those who survive.

**Diagnosis**

Elevation of cardiac troponin I in the setting of SAH seems to be an accurate marker for SAH-associated cardiac dysfunction, with an estimated sensitivity of 100% and specificity of 91%. NSC may be difficult to distinguish from acute MI or myocardial ischemia given the associated ECG changes, wall motion abnormalities, and elevation of cardiac troponin. Potential indicators that favor a diagnosis of NSC include wall motion abnormalities discordant with a single epicardial coronary distribution and a relatively minor troponin release relative to the magnitude of LV dysfunction. One study has shown that among patient with SAH who develop new LV dysfunction, an ejection fraction <40% and troponin T <2.8 ng/mL are predictive of NSC rather than acute MI. Despite these features, coronary angiography may be required to distinguish between NSC and MI in some patients. A proposed algorithm for the evaluation of patients with LV dysfunction associated with SAH is presented in Figure 5.

**Clinical Management**

Clinical management of NSC is generally supportive because LV function usually normalizes spontaneously. Patients should be monitored on telemetry given the risk of arrhythmias, which can be reduced by blocking sympathetic drive. Therefore, β-blocker therapy should be considered early, particularly after a SAH, in which the risk of ventricular arrhythmias is greatest. Surveillance echocardiography is useful to assess for recovery of LV function in those with NSC, which can occur within the first several days. Patients with NSC and brain death are often deemed unsuitable donors for heart transplantation, but this may not be an absolute contraindication to organ donation if rapid recovery of LV systolic function occurs.

**Mechanisms**

The 3 main proposed mechanisms for NSC include the following: (1) ischemic myocardial stunning due to epicardial coronary spasm; (2) ischemic myocardial stunning due to acute coronary microvascular dysfunction; and (3) catecholamine-mediated direct myocardial injury. Epicardial coronary vasospasm is unlikely to be the mechanism for NSC in most cases because it has not been documented during coronary angiography even in patients with persistent ST-segment elevation. Moreover, coronary spasm would not produce the constellation of wall motion abnormalities present in many patients with NSC. Canine models of SAH have not demonstrated microvascular dysfunction or epicardial coronary spasm despite the induction of wall motion abnormalities. Additionally, nuclear myocardial perfusion imaging in humans with NSC has not shown perfusion abnormalities in the acute setting in most patients.

Histological analysis of myocardial tissue in NSC typically demonstrates contraction band necrosis, also known as myocyte lysis, without ischemic necrosis. This finding is consistent with catecholamine-mediated myocardial injury. NSC is
thought by most to represent local myocardial adrenergic toxicity resulting from a centrally mediated sympathetic surge (Figure 6). Experimental stroke models have shown that occlusion of the right middle cerebral artery results in neurochemical derangements in the ipsilateral insular cortex and amygdala, which leads to enhancement of sympathetic outflow to the heart, resulting in an increase in synaptic norepinephrine levels. Enhanced sympathetic outflow can also occur as a result of hypothalamic ischemia in those with SAH, and experimental hypothalamic stimulation can induce cardiac changes similar to those observed in acute cerebrovascular syndromes. Subsequently, norepinephrine hyperstimulation of postsynaptic cardiac catecholamine receptors can enhance myocardial 3',5'-cAMP production, leading to pathological myocyte calcium influx, which prolongs actin-myosin interaction and ultimately results in depletion of energy stores with resultant reduction in ATP generation. The culmination of these events is myocardial injury through contraction band necrosis. Furthermore, patients with NSC have evidence of enhanced peripheral sympathetic activity with increased plasma catecholamine levels, which may also contribute to myocardial toxicity. Animal models of SAH have shown a correlation between peak troponin and peak plasma catecholamine levels. Patients with SAH and NSC exhibit abnormal cardiac sympathetic activity suggestive of functional sympathetic denervation when imaged with the use of meta-iodobenzylguanidine. Experimental interventions such as administration of adrenergic blockers, stellate ganglion blockade, and spinal cord transection can reduce the magnitude of ECG change associated with subarachnoid bleeding and hypothalamic stimulation. A small study found that treatment with propranolol and phentolamine prevents the development of contraction band necrosis in those with SAH, further supporting the catecholamine hypothesis. Similarly, a randomized trial of 114 patients with acute brain injury found that immediate treatment with atenolol reduced the risk of myonecrosis detected by elevation of CK-MB. It has been proposed that the wall motion abnormalities in NSC may result from the differential regional distribution of sympathetic nerve terminal density in the myocardium.

Patients presenting with major ischemic cerebral vascular accidents and severe head trauma can also develop transient wall motion abnormalities that can be associated with ECG changes and mild elevation of CK-MB and troponin. Approximately 10% of those presenting with ischemic stroke have elevated troponin levels, a finding associated with a greater mortality risk. The incidence of myocardial perfusion abnormalities in those with ischemic stroke and troponin
elevation is similar to those without troponin elevation, suggesting a nonischemic mechanism for troponin release in these patients. Patients with ischemic stroke are more likely to have underlying coronary disease, and therefore the relative contribution of preexisting intrinsic cardiac disease to cardiac dysfunction in these patients may be difficult to discern in the acute setting. The distribution of wall motion abnormalities in those with ischemic stroke appears to be quite variable, with global LV dysfunction and apical-sparing LV dysfunction predominating. Apical and midventricular wall motion abnormalities have been reported with ischemic cerebral vascular accidents and head trauma but appear to be relatively uncommon. The differential diagnosis of new-onset systolic cardiac dysfunction in the setting of an ischemic stroke or major head injury should include NSC. These patients should be monitored for potential cardiac complications, and routine assessment for recovery of LV function is recommended.

The similarities between NSC and TC suggest a significant overlap of these syndromes. Both conditions appear, at least in part, to be catecholamine mediated, have a female gender predisposition, present with transient LV wall motion abnormalities in the absence of obstructive CAD, show ischemic-appearing ECG abnormalities, and manifest mild elevations in cardiac biomarkers of myonecrosis. However, notable differences between NSC and TC can be seen in some cases. For example, it appears that a minority of patients with NSC demonstrate isolated apical and midventricular wall motion abnormalities, whereas the majority of TC patients present with this wall motion pattern. In addition, patients with TC appear more likely to present with ST-segment elevation on the ECG compared with those with NSC.

**Transient LV Dysfunction in Acute Medical Illness**

Transient LV systolic dysfunction in the absence of obstructive CAD can occur in patients with acute medical illness, especially those treated in intensive care units. The transient wall motion abnormalities associated with acute medical illness can present as global LV hypokinesis, apical and/or midventricular hypokinesis, or isolated apical and anterior hypokinesis. Several reports have found that sepsis and acute pulmonary illnesses such as exacerbation of asthma appear to be more common precipitants of transient LV dysfunction. A recent study found that 28% of consecutive patients admitted to the intensive care unit for acute medical illness developed transient regional LV dysfunction involving the apical and midventricular segments consistent with TC. Sepsis was the only independent predictor for the development of the stress cardiomyopathy. However, patients in this series did not routinely undergo coronary

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angiography to exclude obstructive CAD as the cause of their LV dysfunction.

Sepsis is a well-recognized cause for transient, global LV systolic dysfunction. It is estimated that up to 50% of patients with severe sepsis develop an associated reversible cardiomyopathy affecting both the left and right ventricles, with recovery of ventricular function within 7 to 10 days if the patient survives the acute phase of the illness.75,79–81 These patients can manifest a minimal troponin release, which portends a greater mortality risk and is associated with greater hemodynamic instability and the need for vasopressor administration for hemodynamic support. Troponin elevation appears to be a sensitive but not specific marker of underlying stress cardiomyopathy in septic patients.81 Although the molecular and cellular mechanisms responsible for transient LV dysfunction in sepsis syndromes are not understood fully, they are likely in part a consequence of the associated intense systemic inflammatory response with the release of tumor necrosis factor-α and other cardiosuppressive cytokines, as well as production of anaphylatoxins such as complement 5a.82 Although microvascular thrombosis has been proposed as a mechanism, the coronary blood flow is preserved in septic patients, and hence myocardial ischemia is unlikely to be a major contributing factor.83 Histopathological studies in patients with LV dysfunction in the setting of sepsis have also shown contraction band necrosis consistent with sympathetically mediated myocardial injury.75 The relative contribution of direct catecholamine myocardial toxicity to LV dysfunction in septic patients is unclear.

Critically ill patients without sepsis can also manifest transient myocardial dysfunction, ECG abnormalities, and troponin release in the absence of obstructive CAD.74,84 Quenot and colleagues74 have reported that 32% of consecutive patients admitted to the intensive care unit with a noncardiac acute medical illness had elevated troponin levels. Overall mortality was 27% in the total population, but those with elevated troponin had a 51% in-hospital mortality compared with 16% without troponin elevation.

LV Dysfunction in Pheochromocytoma and With Exogenous Catecholamine Administration

Transient LV dysfunction can result from endogenous overproduction of catecholamines by neuroendocrine tumors (pheochromocytoma, neuroblastoma) and with the administration of exogenous catecholamines and catecholamine analogues. Pheochromocytoma is a rare tumor of neural crest–derived chromaffin cells that is most commonly located in the adrenal medulla and results in hypersecretion of catecholamines, mainly norepinephrine. The literature on pheochromocytoma-mediated cardiomyopathy, which is largely limited to case reports, indicates that associated cardiac dysfunction is uncommon in the absence of catecholamine crisis and that it resolves after resection of the tumor.85–90 However, subclinical LV dysfunction is found in those with normal LV ejection fraction when assessed by systolic strain rate imaging, and these patients are at increased risk of perioperative hemodynamic collapse.89 The LV wall motion abnormality in patients with pheochromocytoma crisis is generally global in nature, although apical sparing and Takotsubo-like wall motion abnormalities have been reported.90,91 Those with associated LV hypertrophy can develop a dynamic LV intracavitary obstruction with systolic anterior motion of the anterior mitral leaflet during hypertensive crisis.

Transient cardiomyopathy resulting from administration of exogenous catecholamines has been reported.92,93 This has been reported after administration of β-agonists and methylxanthines in those presenting with exacerbations of underlying obstructive airway disease, including asthma, and in those given intravenous and subcutaneous epinephrine in life-threatening situations. Theoretically, the use of high doses of inhaled β-agonist bronchodilators in those with acute pulmonary illness may lead to adrenergic hyperstimulation of the heart with the potential for catecholamine cardiotoxicity. Animal models of exogenous catecholamine toxicity have shown reproducible LV dysfunction, ECG changes, and release of cardiac biomarkers. Acute cocaine intoxication has also been shown to cause myocardial dysfunction with contraction band necrosis.94,95

The transient cardiomyopathy associated with endogenous overproduction and exogenous administration seems to result in part from myocardial catecholamine toxicity as evidenced by contraction band necrosis. As is the case with NSC, these patients have evidence of intracellular myocyte calcium overload due to catecholamine-mediated alterations in calcium homeostasis and associated metabolic derangements that are responsible for myocyte dysfunction.96 Additional potential mechanisms include catecholamine-induced myocarditis and myocardial ischemia caused by a combination of increased myocardial oxygen demand and reduced coronary blood flow due to vasoconstriction.

Conclusion

Stress cardiomyopathy can occur after acute mental or physical stress, SAH, ischemic stroke, major head trauma, acute medical illness, during pheochromocytoma crisis, and as a result of exogenous catecholamine administration (Table 4). The common histological finding of contraction band necrosis in those with stress-induced cardiomyopathy suggests a common catecholamine-mediated mechanism. The relative contribution of other pathophysiological mechanisms such as ischemia remains to be established. Takotsubo cardiomyopathy, a distinct morphological manifestation of stress cardiomyopathy, is characterized by transient systolic dysfunction of the apical and/or midventricular myocardial segments in the absence of obstructive epicardial CAD and is unique in that it can manifest after acute emotional stress. Irrespective of the cause, patients with stress cardiomyopathy with the classic TC morphology deserve special attention because this extensive distribution of wall motion abnormalities has implications for potential associated complications and treatment.

Stress cardiomyopathy is deserving of further research to more precisely explore and understand the underlying pathophysiology of the complex interaction between the brain and the heart, characterize and identify those patients at risk, and develop strategies for preventing this condition. A step in this direction would be to establish a large, centralized interna-
ional registry of stress cardiomyopathy including TC to facilitate further investigative efforts.

**Disclosures**

None.

**References**


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**Table 4. Representative Studies of Stress Cardiomyopathy**

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<tr>
<th>Study</th>
<th>Patient Population</th>
<th>Age, mean ± SD, y</th>
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<th>Global WMA: 9/30 (30%)</th>
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<td>Zaroff et al58</td>
<td>SAH with LV dysfunction/30</td>
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<td>Mayer et al59</td>
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<td>Kono et al54</td>
<td>SAH and ST-segment elevation/7</td>
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<td>Banki et al57</td>
<td>SAH with prospective echo/173</td>
<td>54±13</td>
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<td>Predominantly basal and midventricular involvement with apical sparing</td>
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WMA indicates wall motion abnormality; ICU, intensive care unit.

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**Key Words:** cardiovascular diseases ■ heart failure ■ myocardium ■ takotsubo cardiomyopathy