Takotsubo cardiomyopathy: State-of-the-art review

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Takotsubo cardiomyopathy (TC) is characterized by transient, often severe, left ventricular dysfunction and electrocardiographic changes that might mimic acute myocardial infarction in the absence of significant obstructive coronary artery disease. It is often encountered in elderly women after physical or emotional stress. Excessive catecholamine stimulation, metabolic abnormalities, and microcirculatory dysfunction are thought to be responsible for the manifestations of this disorder. This comprehensive review summarizes relevant published data, atypical presentations, pathophysiology, and management strategy. It also includes a review of 789 patients with TC including nine illustrative cases encountered at our institution.

Key Words: Takotsubo cardiomyopathy • stress-induced cardiomyopathy • left ventricular apical ballooning • myocardial stunning

INTRODUCTION

Approximately 18 years ago, takatsubo cardiomyopathy (TC) was first described in Japan and named after a contraption used for catching octopuses. The disease is also known as left ventricular (LV) apical ballooning, broken heart syndrome, stress-induced cardiomyopathy, and ampulla cardiomyopathy.[1-4] While the initial description was that of reversible aneurysm involving the distal LV myocardium, more recently variant forms limited to mid or basal regions have been described.[5-7]

INCIDENCE

Since first described in 1991 by Satoh and coworkers,[3,8] over 789 cases have been reported in the English literature as of May 2008 (Table 1). TC accounts for 2.2% of all patients admitted with a presumed diagnosis of acute myocardial infarction (MI)[9] and for approximately 2% of patients admitted with decompensated heart failure with electrocardiographic (ECG) changes suggestive of ischemia or MI.[10,11] However, the overall incidence of TC is likely underestimated as this syndrome is frequently overlooked. In fact, transient LV apical ballooning was detected in as many as 23% of patients who were admitted to the intensive care unit and did not have a history of structural heart disease.[12]

PRESENTATION

TC mimics acute MI and is associated with nonobstructive coronary artery disease (CAD) and reversible severe and often extensive regional LV wall motion abnormalities including dyskinesia (aneurysm). These patients usually present with substernal chest pain and ECG changes but with minimal cardiac enzyme elevation. TC primarily occurs in postmenopausal (mean age 68 years) women (87% of reported cases) after a physical or emotional stress.[3] However, a variant presenting as basal ballooning (that spares mid LV region and has paradoxical apical hyperkinesis) has recently been described in young premenopausal women.[13] TC should be considered in all patients with acute chest pain, ischemic ECG changes, and transient LV abnormalities in the absence of severe CAD.

ELECTROCARDIOGRAPHIC CHANGES

While ST-segment elevation in the precordial leads is present in 68% of patients diagnosed with TC (Figure 1A and B), diffuse T-wave inversions are actually the most common ECG finding and are present in 97% of cases.[3,7,14] However, TC is associated with almost every type of ECG abnormality. Patients with TC can

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Table 1. Reported cases of Takotsubo cardiomyopathy in English Literature

Author/ Year	*N*	Women (%)	Age (years)	ST elevation (%)	With emotional or physical stress (%)	Underwent coronary angiography (%)	Without significant CAD (%)	Additional findings
Pavin 1997	2	100	60	0	100	100	100	Two of the earliest reported cases of TC
Sharkey 1998	22	82	56	50	100	59	77	100% of cases had deep T-wave inversion and QT prolongation
Kawai 2000	9	90	66	78	56	100	100	Focal myocyte injury on biopsies without CAD on angiography
Tsuchihashi 2001	88	86	67	90	70	100	100	Vasospasm was induced in 21% of cases and 18% had transient IVPG
Villareal 2001	3	100	69	0	100	100	100	All three with LVOT obstruction, hemodynamic instability, TWI, and QT prolongation
Kurisu 2002	30	93	70	100	33	100	83	No myocarditis by viral titers
Abe 2003	17	82	74	82	94	100	53	Coronary vasospasm was induced in 6% of cases
Desmet 2003	13	92	62	62	69	100	100	LV fxn normalizes in 92% within 3 weeks, but 46% require IABP
Ito 2003	10	70	63	100	70	100	100	Abnormal SPECT MPI during subacute TC despite non-obstructive CAD
Matsuoka 2003	10	90	68	100	100	100	100	Ventricular arrhythmias rarely occur
Ogura 2003	13	69	75	-	-	100	100	In contrast to AMI, ECG in TC has no reciprocal changes but has Q-waves
Seth 2003	12	92	64	-	100	83	100	Role for 2DE in diagnosing TC
Akashi 2004	10	90	73	-	50	100	100	Degree of basal hyperkinesis is correlated with serum BNP
Akashi 2004	8	88	75	100	75	100	100	Increased sympathetic activity on ^{123} I-MIBG scintigraphy despite normal flow
Bybee 2004	16	69	71	81	81	100	100	TIMI frame counts were abnormal in 100% of patients
Ibanez 2004	11	82	72	100	55	45	100	100% of cases involved LAD with a long recurrent segment
Akashi 2005	13	85	74	-	77	100	100	Rarely re-occurs

Table 1. Continued

Author/ Year	*N*	Women (%)	Age (years)	ST elevation (%)	With emotional or physical stress (%)	Underwent coronary angiography (%)	Without significant CAD (%)	Additional findings
Ibanez 2005	5	100	77	-	80	100	100	100% of cases had a ruptured plaque in the mid LAD on IVUS
Inoue 2005	18	61	76	-	50	-	-	ECG distinguishes TC from AMI due to prox LAD but not to distal stenosis
Ito 2005	7	71	63	-	71	100	100	Moderately reduced uptake on ^{123}I-MIBG and ^{123}I-BMIPP at 2 weeks but normal at 1 month
Kume 2005	8	88	71	-	100	100	100	TC is due to coronary microvascular impairment
Park 2005	26	65	63	12	100	-	-	23% of patients admitted to medical ICU have LVAB
Sharkey 2005	22	91	65	59	100	-	-	Shock occurred in 37% of cases, but 100% survived with LV normalization
Wittstein 2005	19	95	58	11	100	100	95	TC is caused by increased sympathetic stimulation and catecholamines
Abdulla 2006	35	100	68	-	-	-	-	Variant with apical sparring, usually occurs in younger women
Azzarelli 2006	8	88	60	50	75	100	100	88% of cases had abnormal TIMI frame counts
Bybee 2006	4	100	71	100	75	100	100	No CAD on angiography but reduced uptake of glucose (F-18 FDG) on PET
Elian 2006	13	92	-	-	62	-	-	LV fxn completely normalizes within 4-5 weeks
El Mahmoud 2006	11	100	70	45	73	100	100	TC has great prognosis
Haghi 2006	47	94	69	-	76	100	100	TC can involve the RV & is associated with depressed LV fxn
Hurst 2006	4	100	53	25	100	100	100	Describes variant involving mid LV
Sato 2006	16	94	72	-	100	-	-	Increased incidence of TC in women living in an area affected by an earthquake

Table 1. Continued

Author/ Year	*N*	Women (%)	Age (years)	ST elevation (%)	With emotional or physical stress (%)	Underwent coronary angiography (%)	Without significant CAD (%)	Additional findings
Akashi 2007	10	80	70	-	80	100	100	TC is due to autonomic imbalance
Bybee 2007	18	100	72	89	-	100	100	ECG changes cannot reliably discriminate between TC and AMI
Fujiwara 2007	11	100	73	55	64	100	100	Distal LV akinesis is not improved by dobutamine infusion
Mitchell 2007	22	100	62	59	82	100	100	During acute TC, no hyperenhancement on CMR despite apical dysfunction
Mitsuma 2007	9	100	74	100	78	100	100	There are four phases of ECG changes in TC
Nef 2007	8	75	71	100	100	100	100	Alterations seen on biopsy during acute TC had complete reversibility after recovery
Patel 2007	5	100	65	80	100	100	100	African-Americans have atypical symptoms; no patient had CP with TC
Reuss 2007	3	100	31	0	100	100	100	Variant involving basal ballooning with mid LV & apical sparing in young women
Angelini 2008	3	100	60	100	100	100	100	Vasospasm induced in 2 cases & other patient had history of prinzmetals angina
Burgdorf 2008	10	90	67	50	80	100	90	Despite normal perfusion of distal LV, uptake of ^{123}I-MIBG severely reduced
Cimarelli 2008	2	100	75	50	-	100	100	^{123}I-MIBG & F-18 FDG defects related to LV abnormalities despite normal perfusion
Fazio 2008	40	85	68	70	-	-	-	7.5% of patients died due to CHF
Meimoun 2008	12	92	68	42	100	100	100	2DE CFR decreased during acute TC but increased at follow-up
Sharkey 2008	59	100	66	56	100	100	100	Patients with TC have similar TIMI frame counts and LV fxn independent of ECG
Virani 2008	4	100	57	50	75	100	100	TC associated with QT prolongation
Yoshioka 2008	34	65	64	74	-	100	100	Propranolol decreases peak gradients in MVO while increasing SBP and LV fxn

Table 1. Continued

Author/ Year	*N*	Women (%)	Age (years)	ST elevation (%)	With emotional or physical stress (%)	Underwent coronary angiography (%)	Without significant CAD (%)	Additional findings
Dorfman 2008	9	89	68	56	89	89	100	2/9 had mid LV variant, 1/9 had recurrence, 1/9 with LVOT obstruction, 2/9 with SVT
	789							

A search engine was performed of citations from the 1950s to May 2008 using PubMed. We used the following search terms: Takotsubo cardiomyopathy and left ventricular apical ballooning and reviewed all related citations and references and citations in the recovered articles. Case series involving two or more consecutive patients were included.

AMI, Acute myocardial infarction; *BMIPP*, B-methy-iodophenyl-pentadecanoic acid; *BNP*, brain natriuretic peptide; *CAD*, coronary artery disease; *CHF*, congestive heart failure; *CMR*, cardiac magnetic resonance imaging; *CP*, chest pain; *CVR*, coronary velocity reserve; *ECG*, electrocardiogram; *FDG*, Fluoro deoxy glucose; *fxn*, function; *IABP*, intra-aortic balloon pump counterpulsation; *ICU*, intensive care unit; *IVPG*, intraventricular pressure gradients; *IVUS*, intravascular ultrasound; *LAD*, left anterior descending artery; *LV*, left ventricle/ventricular; *LVAB*, left ventricular apical ballooning; *LVOT*, left ventricular outflow tract; *MIBG*, metaiodobenzlguanidine; *MPI*, myocardial perfusion imaging; *MVO*, mid left ventricular obstruction; *N*, number of patients; *PET*, positron emission tomography; *SBP*, systolic blood pressure; *SPECT*, single photon emission computed tomography; *TC*, takotsubo cardiomyopathy; *TIMI*, thrombolysis in myocardial infarction; *2DE*, two-dimensional echocardiogram; *SVT*, supraventricular tachycardia.

have ST depression (10%), Q-waves (27%), QT prolongation, and conduction abnormalities such as a new left or right bundle branch block (Figure 1C).[3,7,9,15-18] Patients also tend to present with sinus tachycardia, and the average heart rate at presentation in a recent series was 102 beats/min.[19]

After comparing 33 patients with TC who presented with ST-segment elevation on their ECG to 26 patients with TC who presented with deep T-wave inversions, a recent study concluded that these patients have similar TIMI frame counts and LV function independent of their ECG findings.[20]

In patients with TC and ST elevation, four phases of ECG changes have been described.[19] Phase 1 includes ST-segment elevation during the acute onset; phase 2 includes T-wave inversion on days 1 to 3; phase 3 is characterized by transient improvement in T-wave inversion on days 2 to 6; and phase 4 includes giant deep T-wave inversions and QT prolongation until recovery, which might take up to 2 months.[19]

Several studies have also compared the ECG findings in TC to those occurring as a result of acute coronary occlusion.[16,21,22] While heart rate, PR interval, QRS duration, and QT interval are indistinguishable between patients with anterior MI and TC, ST-segment elevation in the precordial leads might be less prominent in patients with TC.[16,20] In addition, patients with TC do not have reciprocal changes.[21] Nevertheless, it is doubtful that TC can be distinguished from a MI based on ECG changes alone.[16,20,21]

LABORATORY FINDINGS AND PATHOLOGY

Patients with TC usually have evidence of myocardial necrosis; 86% of patients have mildly elevated levels of serum Troponin, and 74% have slightly increased creatine kinase-MB levels.[2,7] Peak troponin levels are significantly lower in patients with TC as compared to those with acute MI.[20] In contrast to the pattern associated with acute MI, the cardiac enzymes in TC peak at presentation and quickly normalize.[3,7,9] Myocardial biopsies done in acute TC have revealed morphological alteration, necrosis, and interstitial fibrosis without infiltration of inflammatory cells.[3,23-26] Evidence for myocarditis is rare, and biopsies are generally inconclusive.[4,23-25,27] However, the alterations seen on biopsy are completely reversible with recovery of LV function.[26]

IMAGING

As the name TC suggests, the most common abnormality in patients with TC is transient LV apical ballooning, which likely results from severe wall motion

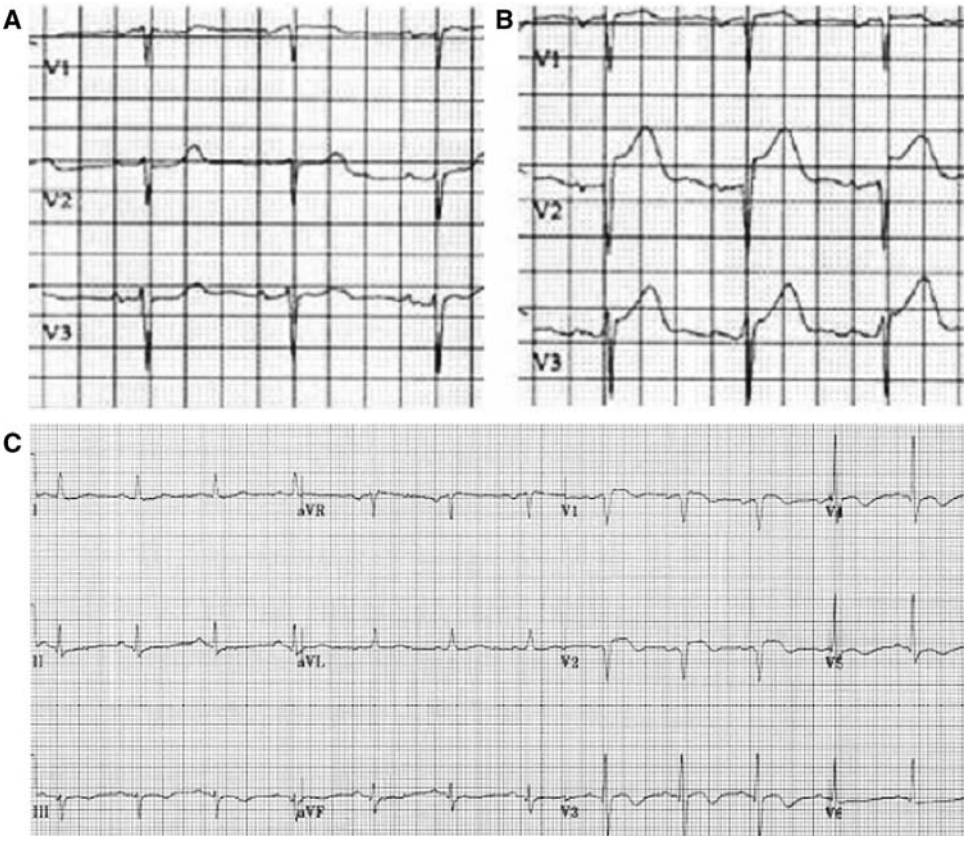

Figure 1. ECG findings in TC. **A**, Baseline prior to TC, **B**, ST-segment elevation during TC, **C**, Combination of new ECG findings such as ST-segment elevation, Q-waves, and diffuse T-wave inversions. Reproduced with modification from Dorfman et al[3] with permission.

abnormality of the distal LV and apex in conjunction with compensatory hyperkinesia of the base. Several variants have been described such as mid LV dyskinesia, basal ballooning with apical hyperkinesis (inverted takotsubo cardiomyopathy), and involvement of the right ventricle.[6,7,13,28] The type with basal ballooning that spares the LV apex is more common in young premenopausal women.[13] Right ventricular involvement is associated with more severe LV dysfunction and a greater likelihood for pleural effusions.[13,28,29] Regardless of the segment involved, the transient wall motion abnormalities, which are the hallmark of this condition, are readily detected by left ventriculography, two-dimensional echocardiography, gated myocardial perfusion imaging, computed tomography, and magnetic resonance imaging (Figures 2-4).[7,30,31]

DIAGNOSIS

The diagnosis of TC requires awareness and sound clinical judgment and is not based on ECG changes or laboratory findings alone. Left ventriculography or a noninvasive imaging modality should be performed in patients with dynamic ECG changes, chest pain, and nonobstructive CAD to detect and to evaluate the characteristic wall motion abnormalites.[20] Recently 4 criteria have been proposed though they lack general acceptance: transient dyskinesis or akinesia of the mid and distal LV with wall motion abnormalities beyond a single major coronary artery distribution; nonobstructive CAD (<50% diameter stenosis) by coronary angiography within 24 h of symptom onset; new ECG changes; and the absence of recent significant head trauma, intracranial hemorrhage, pheochromocytoma, hypertrophic cardiomyopathy, and myocarditis.[14,16]

PATHOPHYSIOLOGY

TC is associated with excessive sympathetic stimulation, microvascular dysfunction, and metabolic abnormalities.[4,23,32-35] Only 5% of patients with TC have significant CAD on coronary angiography. The

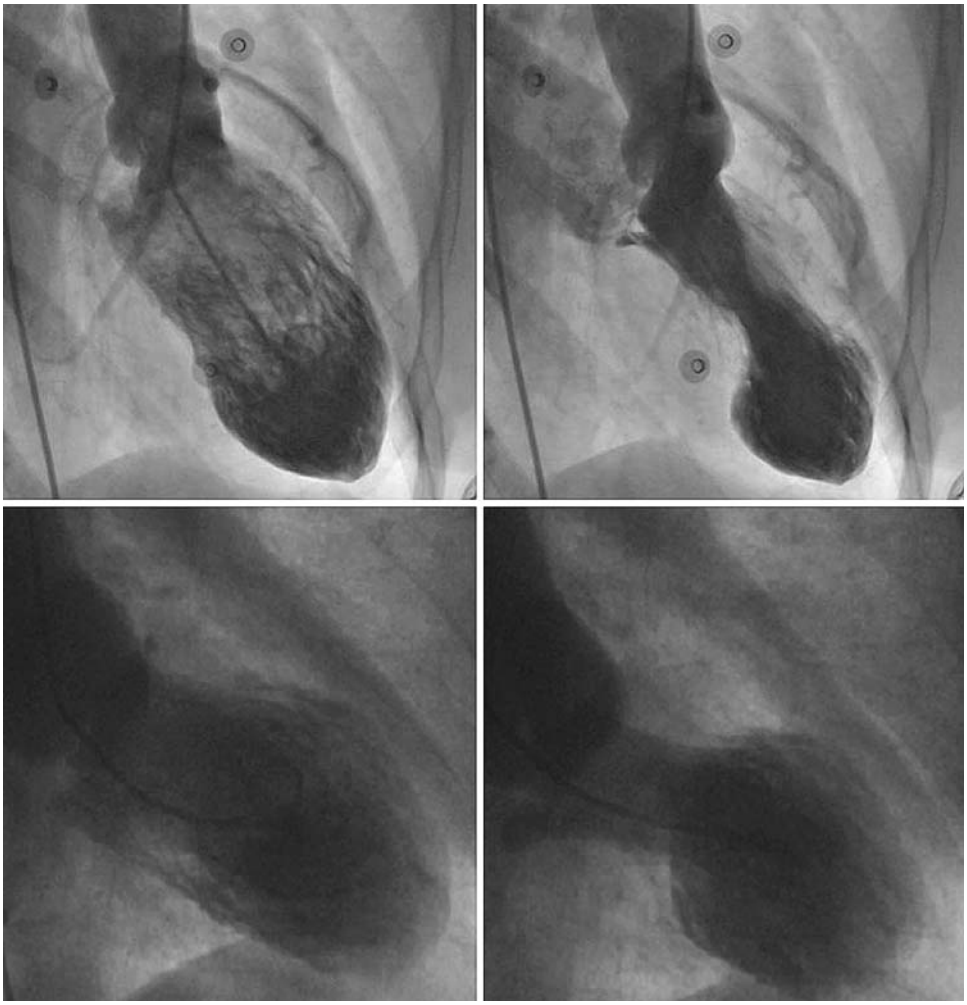

Figure 2. Left ventriculography at end diastole (*left*) and end-systole (*right*) showing the classic appearance of apical ballooning. Reproduced with modification from Dorfman et al[7] with permission.

mechanism leading to wall motion abnormality is poorly understood. Direct myocyte toxicity due to calcium overload, microvascular dysfunction due to excessive catecholamines, or a primary metabolic abnormality are possible targets.[4,33] Plaque rupture or spasm of the left anterior descending artery does not seem to account for most of the cases.[3,36,37] Abnormal myocardial tracer uptake consistent with reduced perfusion has been described in affected LV segments in some patients.[3,4,7,24,35,38] However, the perfusion defects, when present, are much smaller in extent than the distribution of the wall motion abnormalities and could at least be in part due to partial volume effect secondary to reduced thickening.[32] In fact, we recently demonstrated normal perfusion in a patient with TC even when the tracer was injected at the onset of symptoms (Figure 4).[32]

EXCESSIVE SYMPATHETIC STIMULATION

There is evidence that excessive sympathetic stimulation is integral to the development of TC.[3,23,34,39-45] TC has been reported in a few patients after treadmill exercise or dobutamine infusion.[32,46] It has also been described following cocaine and methamphetamine abuse, following inappropriate administration of phenylephrine (neosynephrine), and in patients with thyrotoxicosis and pheochromocytoma.[3,13,47-49] A large systematic review of 542 patients with TC reported that physical or emotional stress was the precipitating factor in approximately 80% of the cases.[3,7]

TC is associated with markedly elevated serum concentrations of catecholamines including nor-epinephrine, epinephrine, and dopamine.[23] Patients with Killip class III or IV on presentation have much higher

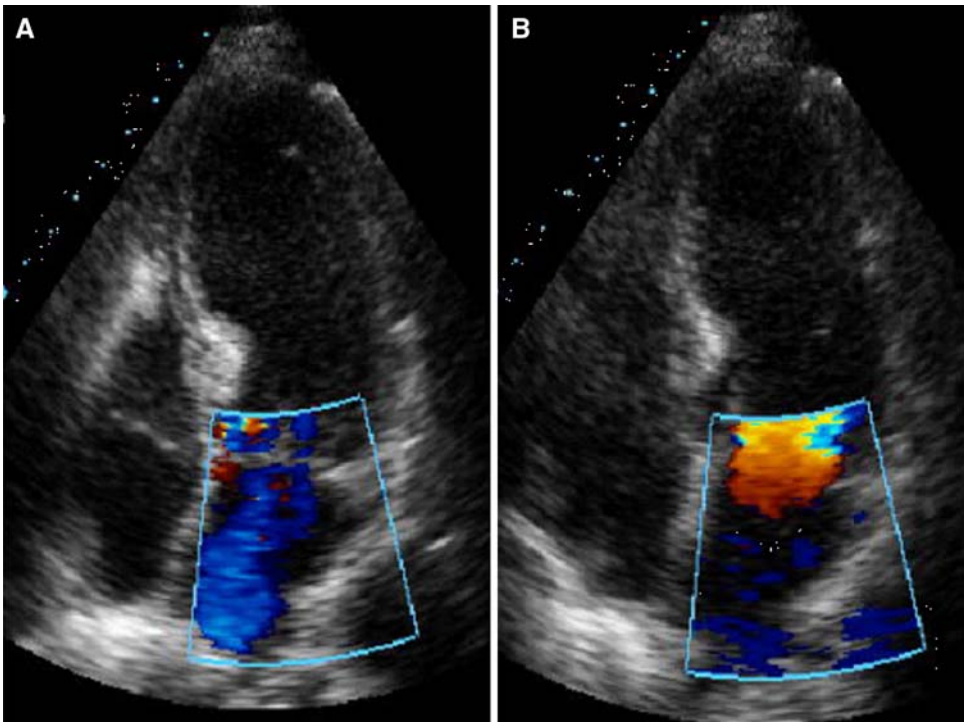

Figure 3. Apical 4 chamber view by two-dimensional echocardiography in **A**, end diastole and **B**, end systole in a patient with TC showing apical ballooning, mitral regurgitation, systolic anterior motion of the anterior mitral valve leaflet, and outflow obstruction.

plasma catecholamine levels than those in Killip class I or II.[8] High levels of catecholamines result in myocyte injury, which is prevented in a large animal model after cardiac sympathectomy.[7,40,41] In rats TC following sympathetic stimulation was not reproducible after administration of alpha- and beta-adrenergic blockade.[34,39]

Neurogenic myocardial stunning has been demonstrated in patients with TC using ^{123}I-metaiodobenzlguanidine (MIBG) myocardial imaging within 3 days of onset, and these changes improved at 3-month follow-up (Figure 5).[10] This tracer has a similar structure, uptake, and storage as norepinephrine and is capable of evaluating cardiac sympathetic activity.[10]

The most common presentation of TC involves the distal LV myocardium, which may be explained by its unique distribution of sympathetic nerves and receptors.[4,33,34,38,39] The greatest density of sympathetic receptors is located in the LV whereas the majority of cholinergic receptors are found in the atria.[3] Of the sympathetic receptors, 85% are either B-1 or B-2, and a-1 and a-2 receptors constitute the remaining 15%.[3] There is an epicardial to endocardial as well as a basal to apical gradient of sympathetic activity.[4,7,33,34,39] Other explanations as to why TC primarily affects the apex include the possible loss of elasticity following extreme expansion and the presence of a thinner layer of myocardium as compared to other regions of the LV.[8]

METABOLIC ABNORMALITIES

Although excessive catecholamine release and enhanced sympathetic stimulation contribute to the development of TC, these patients also have evidence of metabolic impairment and stunning.[4,32,35,50] There is a flow-metabolism mismatch pattern characterized by preserved flow or perfusion (with either N-13 ammonia or Tc-99m sestamibi) and abnormal metabolism (with either I-123 B-methy-iodophenyl-pentadecanoic acid (BMIPP) or F-18 Fluoro deoxy glucose (F-18 FDG) imaging) (Figure 5).[4,35]

Fatty acid metabolism accounts for as much as 80-90% of the energy utilized by the myocardium during rest and aerobic conditions, but fatty acid oxidation is severely suppressed and replaced by glucose metabolism during ischemia.[32,35,38] In TC, glucose utilization and the degree of abnormality in fatty acid metabolism is out of proportion to the degree of abnormal myocardial perfusion (if any) in the affected segments.[35,38]

In contrast to the pattern observed in patients with acute MI, myocardial perfusion is relatively preserved in TC despite a marked reduction in the uptake of glucose

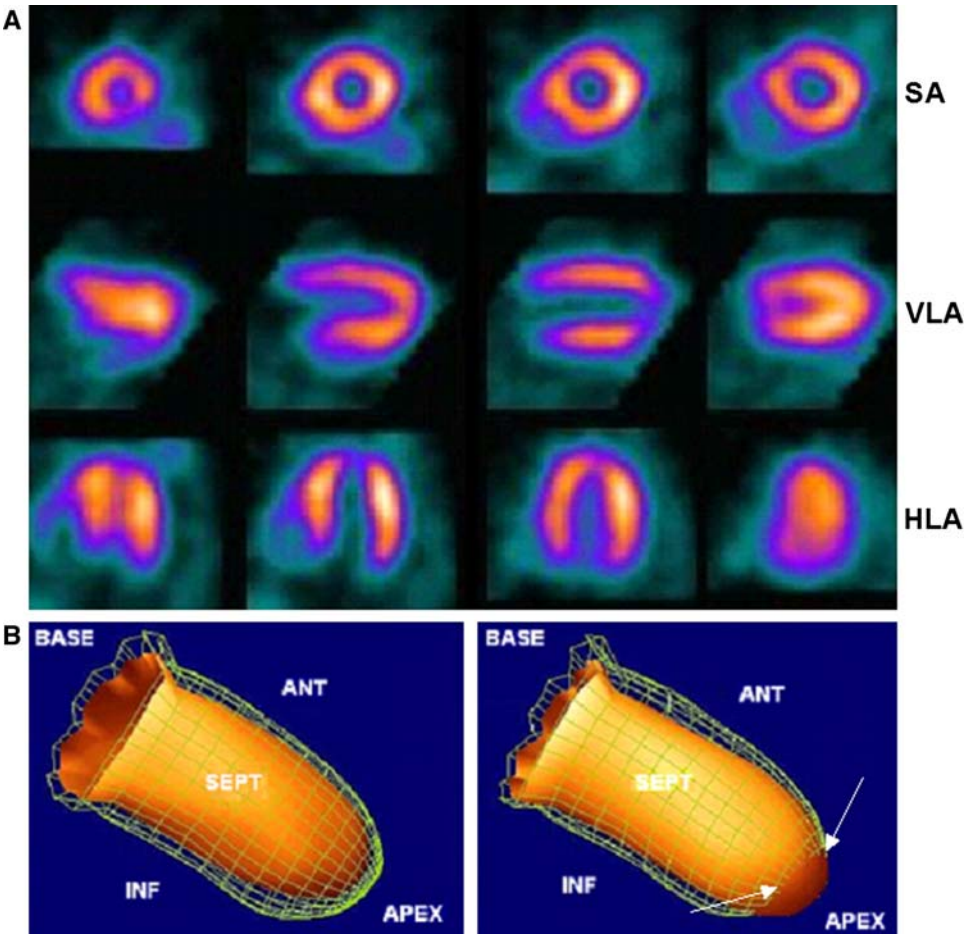

Figure 4. Normal perfusion pattern in a patient who developed TC during treadmill exercise testing when the tracer was injected at the onset of the disorder (**A**). The gated images show apical dyskinesia despite normal perfusion (**B**). Reproduced with modification from Dorfman et al[32] with permission.

(features of myocardial stunning),[4,9,32,35] and unlike stunned myocardium following ischemia due to epicardial coronary stenosis, distal LV akinesis is not improved by low-dose dobutamine infusion in patients with TC.[51]

The etiology of the impairment in glucose metabolism is unclear, but insulin resistance has been associated with high levels of catecholamines.[4,32,50] There is also a reduction in several enzymes involved in the glycolytic pathway, and patients with TC might have decreased sensitivity to calcium, which results in diminished translocation of glucose transporter-4 from the sarcolemma to the intracellular pool.[4,32]

MICROCIRCULATORY DYSFUNCTION

A recent review of 30 patients with TC reported that coronary vasospasm occurs in one out of three patients[27] and can be induced in an additional 14% to 21% of patients.[17,24,25] Out of the nine patients diagnosed with TC at our institution in the past 22 months, one (11%) had evidence of severe coronary spasm relieved by nitroglycerin.

However, large vessel spasm does not account for the majority of cases.[4,10,27] The largest single center experience to date consisted of 88 patients with TC, and none of the patients had evidence of spontaneous large vessel spasm.[17] While there might be a weak relationship between TC and Prinzmetal angina,[52] the primary vascular disturbance in these patients is more likely secondary to microvascular dysfunction.[9,34,35,53-55] In a recent study including 16 women with TC, 100% of patients had abnormal TIMI frame counts, which frequently involved all three major coronary arteries.[9] During acute episodes of TC, there is a reduction in coronary flow velocity reserve and a decrease in the time of diastolic velocity deceleration, which improved at 3-week follow-up.[34,54] Another study using two-

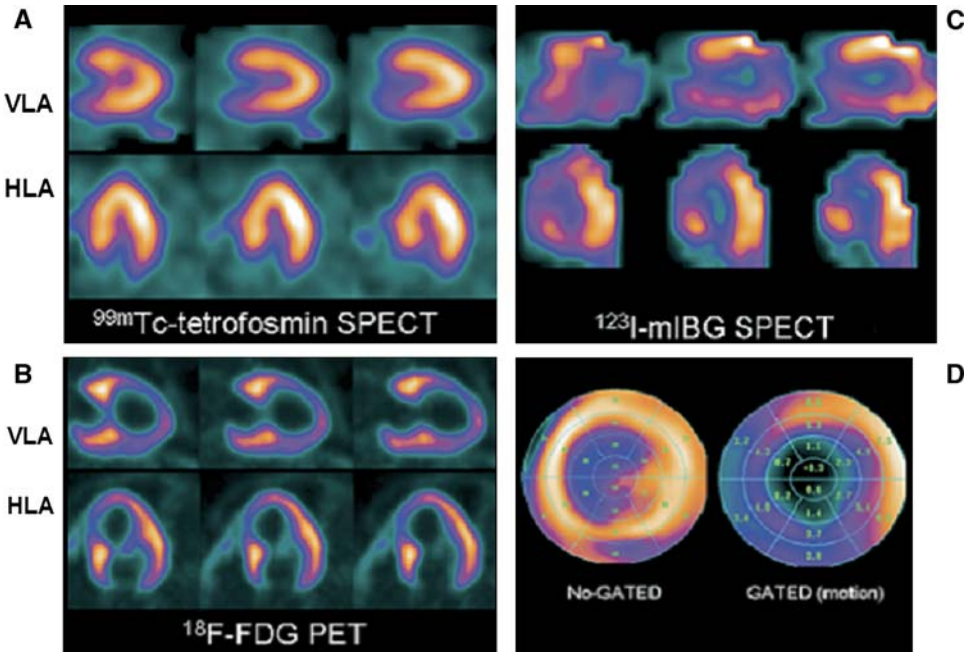

Figure 5. Myocardial perfusion images with Tc-99 m tetrofosmin SPECT (**A**), F-18 FDG PET images (**B**), and I-123 MIBG images (**C**) in a patient with TC. The metabolic and sympathetic images are abnormal, but the perfusion images are normal. There is contractile dysfunction (**D**). Reproduced with modification from Cimarelli et al[31] with permission.

dimensional echocardiography demonstrated that coronary flow reserve increased in 100% of patients with TC from the time of presentation to complete recovery at 25-day follow-up, and there was also a significant correlation between the increases in coronary flow reserve and improvement in the degree of wall motion abnormalities.[54]

HORMONES

There is minimal data addressing the role for hormones in the development of TC though 87% of the reported cases are encountered in postmenopausal women.[3,7] Low estrogen levels are reported to contribute to myocardial stunning.[7] Rats with bilateral ovariectomies are more susceptible to TC after physiological stress, and myocardial stunning in small animal models is diminished following administration of estrogen.[7,40] TC has been described in a 31-year-old healthy female following an elective cesarean delivery with complete recovery of LV function within 4 weeks suggesting that some cases of peripartum cardiomyopathy might be examples of TC. Here again, excessive sympathetic stimulation due to pain may be the trigger mechanism.[56] Further investigation into a possible relationship is warranted. Although TC is always reversible, both conditions are associated with changes in hormones, marked sympathetic stimulation, and LV dysfunction.

COMPLICATIONS

Chest pain is the most common presentation of TC, but patients can present with dyspnea, heart failure, or new ECG abnormalities. Several severe complications can also occur. According to a systematic review of 206 patients with TC, 27% had heart failure, 18% required inotropes, and 13% were stabilized with an intra-aortic balloon pump.[7] LV free wall rupture, LV thrombus, LV outflow tract obstruction with systolic anterior-motion of the mitral valve leaflet, mitral regurgitation, ventricular arrhythmias, and death have rarely been reported.[9,14,17,41,57]

Of the nine patients diagnosed with TC at our institution within the past 12 months, one had cardiogenic shock secondary to LV outflow obstruction with systolic anterior motion of the mitral valve and a 50 mmHg gradient across the LV outflow tract (Figure 6).[7] Only 2% of patients with TC have transient LV outflow obstruction,[7] but transient intraventricular pressure gradients are found in as many as 16% of cases.[2,7,9,17,58]

Mid and distal LV akinesia with compensatory basal hyperkinesia can cause LV cavity obliteration,

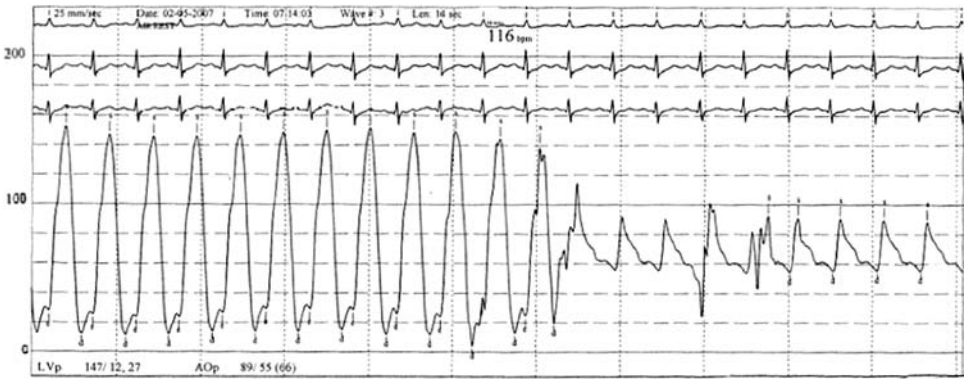

Figure 6. LV pressure measurements showing a large gradient across the LV outflow tract in a patient with TC. This patient presented with cardiogenic shock but made a complete recovery.

which results in LV outflow obstruction and intraventricular pressure gradients.[7,14,41] Small LV volume, small outflow area, and a sigmoid septum (septal bulge) are risk factors for the development of transient outflow obstruction especially in the presence of enhanced sympathetic activity or severe hypovolemia.[7,41,59] Outflow obstruction and transient intraventricular pressure gradients are also associated with dobutamine administration.[7,8,30,46]

TREATMENT

Management of TC is primarily empirical, but there is emerging data supporting the role for beta blockade in this setting.[2,7,8] Treatment should be individualized as patients with dynamic intraventricular pressure gradients and outflow obstruction require different management than patients presenting with hypotension secondary to depressed LV function.[7,14,41,58] Propranolol decreased peak gradients (90-22 mm Hg) in patients with midventricular obstruction while increasing both systolic blood pressure (85-116 mm Hg) and LV ejection fraction (30% to 42%).[8]

There is evidence that dobutamine is contraindicated in patients with TC especially in the presence of outflow obstruction, and the safety and utility of intraaortic balloon pump counterpulsation has also been questioned.[7,30,46]

Beta blockers and alpha-adrenoceptor agonists such as phenylephrine attenuate transient outflow obstruction.[7,41] Beta blockers also decrease LV contractility and increase the time of diastolic filling, which augments LV volume at end diastole and outflow area.[7,14,41,58] By increasing afterload, phenylephrine attenuates both intraventricular pressure gradients and ejection velocity, and these changes result in a higher LV end diastolic volume.[7,14,41,58] Dihydropyridine calcium channel blockers are recommended in patients with TC with evidence of coronary artery vasospasm instead of beta blockers and phenylephrine.[7,14] The role for aspirin and angiotensin-converting enzyme inhibitors is unclear but not discouraged.[7]

PROGNOSIS AND RECURRENCE

Takotsubo cardiomyopathy is generally a benign condition; in-hospital mortality is <1%, and death is much more common in the setting of outflow obstruction and inappropriate management.[2,7,14,46,60] There is no permanent myocardial necrosis, and contrast-enhanced magnetic resonance imaging often fails to show residual scarring despite severe regional dysfunction.[61] Moreover, morphological alterations seen on myocardial biopsy completely normalize after functional recovery.[26]

Serum NT-pro BNP and catecholamine levels at presentation correlate with Killip class heart failure and associated complications, and low levels predict favorable outcomes.[8,11,62] However, the utility of these biomarkers is unclear given the fact that TC generally has a favorable long-term prognosis.[2,14,63-65] The data on recurrence is limited and is likely rare but might be slightly more common in young women with variants that spare the distal LV myocardium.[2,7,14,29,66]

CONCLUSION

Stress-induced cardiomyopathy most commonly affects postmenopausal women and is characterized by symptoms, new ECG changes, and transient often severe regional LV dysfunction in the absence of obstructive CAD. The diagnosis requires awareness and recognition of characteristic wall motion abnormalities. The etiology is likely due to excessive sympathetic activity, metabolic and microcirculatory stunning, and low estrogen levels. The prognosis is generally favorable with complete recovery of LV function, but complications such as

outflow obstruction and heart failure occur and require prompt diagnosis and optimal management.

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