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Takotsubo Cardiomyopathy vs. Acute Coronary Syndrome in the Emergency Department Setting: a Review of Diagnostic Criteria and Outcomes

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Abstract
Purpose of Review The purpose of this article is to review the Mayo Clinic criteria for diagnosis, differential diagnoses, epidemiology, pathogenesis, imaging, treatment, and prognosis for this condition.
Recent Findings Takotsubo cardiomyopathy (TCMP) often poses a diagnostic dilemma in the emergency department (ED) and in the intensive care unit (ICU) setting. TCMP is virtually indistinguishable from acute coronary syndrome (ACS).
Summary Further research is needed to study the pathogenesis of this condition and to investigate whether genetic or serologic markers could be used to identify individuals at risk for this condition.

Keywords Takotsubo · Cardiomyopathy · Acute coronary syndrome

Introduction: Nomenclature and Historical Perspective

Takotsubo cardiomyopathy (TCMP) was first recognized in Japan in 1990 [1, 2]. It is known by various names: stress induced cardomyopathy, apical ballooning, and broken heart syndrome. The term takotsubo means an octopus trap in Japanese, as the left ventricle (LV) during systole assumes the shape of one. While the mid to apical segments are hypokinetic, the base is hypercontractile. TCMP is characterized by transient, regional wall motion abnormality (WMA) which extends beyond the perfusion of a single coronary artery [1–3, 4••, 5•].

Moreover, the WMA occurs in the absence of obstructive coronary artery disease (CAD) supplying this territory [4••, 5•, 6].

Clinical Presentation

Acute onset of substernal chest pain is the most common presenting symptom to the emergency department (ED), while others may present with dyspnea, acute heart failure, tachyarrhythmia, bradyarrhythmia, sudden cardiac death, left ventricular outflow (LVOT) obstruction, or acute mitral regurgitation. LVOT obstruction is due to basal hyperkinesis. Patients with LVOT obstruction may present with a late systolic murmur and shock. Ten percent of patients suffered cardiogenic shock. Transient ischemic attack and stroke have also been reported [3, 4••, 6–10].

Criteria for Diagnosis

The diagnosis of TCMP may be suspected if the clinical severity exceeds the degree of cardiac biomarker elevations, but this diagnosis is generally not made in the ED, as the presentation is indistinguishable from ACS, and requires sequential assessment of ventricular systolic function, usually with echocardiogram, to confirm that the ventricular dysfunction is transient [4••, 5•, 11].

The current diagnosis of CMP requires meeting all four of the Mayo Clinic criteria for diagnosis [11, 12].

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1. New EKG abnormalities, which may include ST elevation or depression, T wave inversion, QT prolongation, or non-specific STT abnormalities
2. Absence of obstructive coronary artery disease (CAD) in the distribution of the wall motion abnormality
3. Transient left ventricular wall motion abnormalities extending beyond a single coronary artery distribution
4. Absence of pheochromocytoma and myocarditis

Epidemiology

One to two percent of acute myocardial infarctions have been retrospectively reclassified as TCMP after coronary angiography and sequential assessment of the left ventricular systolic function [6, 9, 11]. It tends to affect older women, with a mean age of 66.4 years. 89.9% of TCMP has been diagnosed in women [4••].

While the nomenclature implies stress, an international registry identified physical stress in 36%, emotional trigger in 27.7%, and combined trigger in 7.8% of patients. In 28.5%, no trigger was identified [4••]. Fifteen percent of patients in the international registry were recognized as having concomitant CAD [4••, 11].

Pathogenesis

The etiology of TCMP is unknown. It has been postulated that catecholamine-induced myocardial stunning, coronary spasm, or microvascular dysfunction as potential mechanism for causing transient ventricular dysfunction. Increased plasma norepinephrine was found in 26 of 35 patients (74%) in one study [5•, 7, 8, 12, 13]. However, plasma catecholamine levels have not been found to be uniquely higher in TCMP vs. ACS patients in another study [14]. Abnormal TIMI frame counts, suggestive of coronary vasospasm during coronary angiography has also been reported [15]. One study reported a preponderance of chronic affective or neurologic disorder, such as anxiety, headaches, and seizures, in 55.8% of patients with TCMP, vs. 25.7% of patients with ACS [4••]. Genetic predisposition has also been observed [16–21].

Diagnostic Testing and Treatment

The initial testing and treatment for TCMP should be the same as for ACS. EKG, cardiac biomarkers, B-type natrieuretic peptide or NT pro-BNP, and chest X-Ray should be obtained immediately upon arrival to the ED [4••, 5•, 12]. Coronary angiography (CA) should be undertaken as soon as possible in the appropriate patient. If the criteria are met for ST elevation myocardial infarction (STEMI) and CA is not available, thrombolytic and antiplatelet therapy should be initiated immediately. Beta blocker is also indicated as acute treatment. However, there has not been any data on long-term benefit of beta blocker, as 50% of patients with recurrent TCMP were taking beta blocker [22•]. Heart failure and dysrhythmia should be treated with conventional therapy for these conditions.

Echocardiogram showed mid to apical hypokinesis, akinesis, or dyskinesis in 81.7% of patients. These individuals exhibited basal hyperkinesis. 14.6% had mid ventricular, 2.2% had basal, and 1.5% had anterolateral hypokinesis. Mean LVEF was 41% [4••]. One third of patients had combined left and right ventricular (RV) systolic dysfunction [4••, 6, 7, 23–25]. Those with combined LV and RV systolic dysfunction tend to have a lower LVEF of 40%, vs. 48% in patients with sole LV involvement [25].

Cardiac magnetic resonance imaging (CMR) may also be considered for distinguishing TCMP from myocardial infarction (MI) and myocarditis. In MI, there is intense subendocardial or transmural late gadolinium enhancement (LGE). In myocarditis, LGE is usually in a patchy distribution. In TCMP, LGE is absent. Myocardial edema is less common in TCMP than in MI and myocarditis. CMR is also helpful in identifying cardiac thrombus and RV involvement [24, 25].

Positron emission tomography (PET) can also be used to distinguish TCMP from myocardial infarction (MI), as the former will show normal perfusion and reduced glucose utilization, known as an inverse flow metabolism mismatch, whereas in MI, both perfusion and glucose utilization are reduced [26].

Differential Diagnoses

Other conditions mimicking TCMP include cocaine-induced ACS, distinguishable through toxicology; myocarditis, which has a slower recovery than TCMP; and pheochromocytoma, a condition where patients often exhibit tachycardia, sweating, headaches, and weight loss [27].

Prognosis

TCMP patients who show RV involvement tend to have a lower median LVEF of 40% (vs. 48%), and a more serious condition. Cardiogenic shock is more common in this subgroup.

Of 18,353 patients with TCMP, 4.1% died in the hospital (7.5% were men, 3.8% were women). They tend to be older men with peripheral arterial disease (PAD), had ventricular fibrillation or cardiac arrest, and lived in the northeast region

[28]. Asians also have a higher mortality rate amongst various ethnic groups [29].

Conclusion and Summary

TCMP is indistinguishable from ACS upon presentation to the ED, and should be treated as such. Unlike ACS, the severity of this disease exceeds the level of biomarker elevation, and ventricular function recovers rather quickly, generally over the course of a week [30]. Mayo Clinic diagnostic criteria, imaging modalities, and clinical course distinguish TCMP from ACS, myocarditis, and pheochromocytoma. Older age, PAD, male gender, ventricular fibrillation, cardiac arrest, and RV involvement are predictors for a higher in-hospital mortality rate. While TCMP should be treated like heart failure with reduced EF, chronic beta blocker usage has not been observed to reduce the recurrence of this disorder [22•].

Compliance with Ethical Standards

Conflict of Interest Dr. Hui declares no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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