Takotsubo Cardiomyopathy
Definition and Clinical Profile

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KEYWORDS

• Apical ballooning syndrome • Takotsubo cardiomyopathy • Stress cardiomyopathy

KEY POINTS

- Takotsubo cardiomyopathy (TTC) is an increasingly recognized, reversible cardiomyopathy with a clinical presentation that mimics an acute coronary syndrome (ACS).
- TTC is estimated to represent 1% to 2% of patients presenting with suspected ACS, most commonly manifests in postmenopausal women, and is precipitated by emotional or physical stressors in a majority of cases.
- Typical presentation involves chest pain and/or dyspnea, transient ST-segment elevation on the electrocardiogram, and a modest increase in cardiac troponin.
- Cardiac imaging demonstrates wall-motion abnormalities that generally extend beyond the territory of a single epicardial coronary artery, and the absence of obstructive coronary lesions.
- Supportive treatment typically leads to spontaneous, rapid recovery of ventricular function within weeks.

INTRODUCTION

Takotsubo cardiomyopathy (TTC), also known as stress-induced cardiomyopathy, apical ballooning syndrome, and broken heart syndrome, is an increasingly recognized transient condition that results in a characteristic pattern of ventricular systolic dysfunction frequently precipitated by a stressful event.[1–4] The syndrome was initially reported in Japan in 1991 and was named "takotsubo" after the round-bottomed and narrow-necked octopus trap that resembles the apical ballooning systolic morphology of the left ventricle in the classic form of TTC.[5] Since then there have been several case series reported from North America,[6–13] Europe,[14–17] Asia,[18–20] and Australia,[21] and TTC is now recognized as a primary acquired cardiomyopathy in the American Heart Association scientific statement on the classification of cardiomyopathies.[22] In the typical form of TTC, the systolic contractile dysfunction involves the mid and apical segments of the left ventricle with compensatory basal wall hyperkinesis.[2] Atypical forms involving basal or midventricular hypokinesis with apical sparing have been reported less commonly.[14,15,21,23–25] TTC is unique in that it disproportionately occurs in postmenopausal women,[4,7,14,20] and in a majority of cases is preceded by an acute physical or emotional stressor.[4,7,9,17,20] The pathophysiology of TTC is not well understood, but postulated mechanisms include catecholamine excess, either with direct myocardial toxicity or through induction of microvascular dysfunction or coronary spasm.[26,27]

Although there has been increasing recognition of this unique syndrome, TTC is often misdiagnosed

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as an acute coronary syndrome (ACS) given the similarities in the clinical presentation, electrocardiographic features, and cardiac biomarker profile; however, the cardiomyopathy virtually always occurs in the absence of flow-limiting coronary atherosclerosis. Thus it is an important differential diagnosis of acute myocardial infarction, and is estimated to represent approximately 1% to 2% of patients presenting with suspected ACS.[2,4,19,28] In a recent analysis from the Nationwide Inpatient Sample discharge records in the United States for the year 2008 using the *International Classification of Diseases, Ninth Revision,* code 429.83, the incidence of TTC among all hospitalizations in the United States was estimated to be approximately 0.02%.[29]

CLINICAL CHARACTERISTICS

Patient Demographics and Associated Factors

Most patients with TTC (80%–100%) are postmenopausal women with a mean age of 61 to 76 years, based on published case series.[4,7,14,27,30] TTC is uncommonly (<3%) reported in individuals who are younger than 50 years.[27] The exact incidence of TTC is unclear given the similarity to and misdiagnosis as ACS, but is estimated to account for 1.7% to 2.2% of cases presenting with suspected ACS.[27] A preceding emotional or physical stress is a unique feature of TTC, with approximately two-thirds of cases having associated, identifiable acute stressors.[10,27,31] A variety of emotional stressors has been reported, including the death of a loved one, natural disasters, financial loss, and domestic violence.[10,27] Physical stressors reported include acute critical illness (intensive care unit population without known cardiac diagnosis), postoperative state, severe pain, exacerbations of chronic obstructive pulmonary disease or asthma, as well as central nervous system disorders such as seizures, subarachnoid hemorrhage, and posterior reversible encephalopathy syndrome.[7,27,32–36] A comprehensive list of associated triggers are detailed in **Box 1**. Of importance, the absence of a precipitating stressor does not preclude a diagnosis of TTC, as up to one-third of patients do not have identifiable preceding triggers.

A genetic predisposition has been implicated with the report of familial cases of TTC.[107,108] Compared with the general population, TTC patients are more likely to have a chronic anxiety disorder or have a family history of psychiatric disease, thus implicating premorbid psychiatric disease as a possible predisposing factor.[109] The reason for a predominance of postmenopausal female patients is unknown. One study noted that compared with women, men more often developed TTC during or immediately after receiving medical therapy or an examination for a noncardiac medical illness (ie, in response to a physical trigger), suggesting sex differences in the types of TTC-provoking events.[110] Another study found higher concentrations of estradiol in postmenopausal TTC patients than in women with acute myocardial infarction and women with normal coronary arteries, with the investigators postulating that estradiol in these women exerts an atheroprotective effect diverting stress responses from ACS to TTC.[111]

Presenting Symptoms and Complications

Chest pain, which has the characteristics of angina, is the most common presenting symptom and has been reported in as many as 60% to 100% of patients among published series of patients.[10,31,35] Dyspnea is also a common symptom, and less frequently patients present with other symptoms such as syncope or cardiac arrest. A small proportion of asymptomatic patients are identified after ischemic changes on the electrocardiogram (ECG) or when cardiac biomarker elevations are noted during hospitalization for a noncardiac illness.[10,31,35]

Acute heart failure, manifesting as pulmonary edema, occurs in up to 45% of patients, and cardiogenic shock necessitating intra-aortic balloon counterpulsation (IABP) occurs in up to 20% of cases.[30,112] Other complications include dynamic left ventricular outflow tract obstruction (~10%–15%) and acute mitral regurgitation caused by transient valve dysfunction.[10,27,113,114] Rare complications include thrombus formation along the dyskinetic ventricular walls (typically seen in <5% of patients)[10] and cardiac rupture.[115]

Electrocardiogram

ECG changes of ischemia or injury are the most common clinical finding in TTC, with transient ST-segment elevation present on the initial ECG in 30% to 50% of patients.[10,18–20,31,37,116–118] The transient ST-segment elevation attributable to TTC cannot be distinguished from the findings in patients with an ST-segment elevation myocardial infarction, and most commonly involves the precordial leads.[119] Reported ECG diagnostic criteria for distinguishing the 2 conditions have not been validated and have limited diagnostic accuracy.[119–121] The extent and magnitude of ST-segment elevation on the electrocardiogram may be correlated with the likelihood of in-hospital complications.[122] Widespread, deep T-wave inversions in the precordial leads are noted at presentation in some patients, and develop over the course of 2 to 3 days in others (**Fig. 1**).