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Takotsubo Syndrome: Is It Just a "Broken Heart"?

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Takotsubo syndrome (TTS), also known as stress-induced cardiomyopathy, is characterized by reversible ventricular dysfunction without evidence of acute coronary artery occlusion on angiography.[1] The etymology of the word "Takotsubo" traces to a type of pot with a narrow neck and round bottom used to catch octopus, and was used to describe the morphology of the left ventricle with regional wall motion abnormalities seen on echocardiogram. Hence, TTS is also called "apical ballooning syndrome". While the prevalence of TTS remains mixed across various studies, it is estimated that TTS accounts for 1%−3% of cases of acute coronary syndrome (ACS).[2,3]

TTS is classified as either primary or secondary based on patient presentation. Primary TTS occurs as an initial presentation with acute onset chest pain or dyspnea with concern for ACS, electrocardiogram (ECG) may show ST-segment elevation or depression, prolonged QT interval, and T wave inversion. It is usually not localized to a single coronary artery region. However, angiography reveals clear coronary arteries or nonocclusive disease inconsistent with regional wall motion abnormalities.[3,4] It may be idiopathic but is often attributed to emotional or psychiatric stress, giving way to the more colloquial term "broken heart syndrome" (5). Secondary, TTS occurs as a complication of a pre-existing medical or surgical condition, including but not limited to sepsis, trauma, stroke, and intracranial hemorrhage.[6]

While specific risk factors for TTS are difficult to identify, studies have been done comparing mortality and morbidity based on age, sex, comorbidities, and trigger events. Although TTS is more common in females, with 80%−90% of cases occurring in older women, most studies found that females have more favorable short-term outcomes compared to their male counterparts, though the difference in long-term effects is still unclear.[1,5] A large National Inpatient Sample database study showed that the average age for males with TTS was lower than females, with >20% male patients aged less than 35 years.[7] Male patients were also found to have significantly higher rates of in-hospital mortality, admission to the intensive care unit, and frequency of severe heart failure, ventricular arrhythmias, acute kidney injury, and cardiogenic shock.[7,8] This disparity may be attributed to estrogen having a cardioprotective effect, which may also explain higher prevalence in postmenopausal females. It is theorized that the effects of catecholamine surge in TTS leading to myocardial stunning and microvascular dysfunction is diminished by estrogen due to modulation of cardiovascular reactivity by increasing vagal tone and decreasing sympathetic activity.[9]

Prognostication may also depend on the triggering event, which can be either emotional, physical, or unclear. Physical triggers can include underlying medical conditions, trauma, infection, hypoxia, neurologic events, or even extreme physical activity. A study based on the Spanish National Registry on Takotsubo Syndrome (RETAKO) found that patients with physical or no identifiable triggers had worse outcomes than those with emotional triggers, including longer hospital stay and lower ventricular function, with hypoxia-triggered TTS having the highest short- and long-term mortality.[6] Pre-morbid state is also important to take into consideration, with diabetes mellitus (DM), chronic kidney disease (CKD), heart failure with reduced ejection fraction <30%, and malignancy were all associated with more long-term mortality.[2] CKD with eGFR <30%, in particular, was associated with higher incidence of adverse effects, including acute kidney injury with severe renal impairment, recurrent TTS, and increased need for inotropes in management.[10] Given the connection

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between primary TTS and emotional stress, more investigations are being done to find associations with psychiatric disorders, with the premise that exacerbations can be identified as potential triggers and therefore prevented, however the current data is equivocal, and the effect of underlying psychiatric disease on prognosis continues to be unclear.[1,2]

With increasing prevalence of TTS, trends in imaging and biomarkers can be analyzed.

Troponins and CK-MB are elevated in both TTS and ACS, however TTS has lower peak levels of cardiac enzymes compared to ACS.[11] Brain natriuretic peptide (BNP) has been found to be higher in TTS, possibly due to left ventricular ballooning and sudden focal loss on contractility leading to increased filling pressures. The BNP/troponin ratio can be useful in differentiating TTS from ACS as it is significantly higher in TTS, however no specific biomarker has yet been validated.[12] Interestingly, elevated BNP and detectable troponin levels were often found to be persistent after the initial insult in TTS.

Transthoracic echocardiography is considered to be gold-standard in the acute phase, particularly in describing the pattern of ventricular ballooning. Lower left ventricular ejection fraction (LVEF), higher left ventricular end-systolic and end-diastolic volumes are associated with higher likelihood of short-term adverse events including acute heart failure, cardiogenic shock, supraventricular and ventricular arrhythmias, and cardiac death.[12] Low LVEF and higher wall motion score index, which describes a higher degree of hypokinesia, are particularly associated with pulmonary edema, cardiogenic shock and hemodynamic instability.

Despite its reversible nature, TTS can lead to complications including arrhythmias, acute heart failure, cardiogenic shock, ventricular thrombus and risk for cerebrovascular events, with significant morbidity and mortality if not promptly diagnosed and managed. Therefore, prognostication for TTS is crucial for identifying patients at higher risk of adverse outcomes.

Author contributions

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Ethics approval and consent to participate

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Conflicts of interest

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