

EDITORIAL COMMENT

Role of Echocardiography in Tako-Tsubo Cardiomyopathy Beyond Diagnosis?*

John D. Horowitz, MBBS, BMEDSCI(HONS), PHD, Thanh H. Nguyen, MD, MMEDSCI, PHD
Adelaide, Australia

Tako-tsubo cardiomyopathy (TTC) is characterized by the acute onset of segmental systolic dysfunction of regions of the left (and sometimes the right) ventricle, associated with various degrees of chest discomfort and/or dyspnea (1). Differentiating TTC from acute myocardial infarction may present a challenging task, requiring a combination of echocardiography, cardiac catheterization, and subsequent cardiac magnetic resonance (CMR) evaluation (2).

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Most TTC patients are aging women, and in most cases, attacks are precipitated by severe physical or emotional stress. It has become clear that an “aberrant” cardiac response to catecholamine stimulation initiates TTC episodes: indeed, as TTC may also be induced by medical administration of catecholamine, there are some obvious therapeutic priorities associated with the diagnosis, even though the precise signal transduction cascade initiated by catecholamine exposure remains only partially elucidated (3). Furthermore, TTC is characterized by both myocardial and systemic inflammatory activation, demonstrable on CMR (4) and via “non-congestive” release of B-type natriuretic peptide (BNP) (5).

There is increasing evidence that TTC is not necessarily benign either in the short or long term. Although the absolute risk of early life-threatening tachyarrhythmia remains uncertain, it is clear that many patients develop substantial hypotension in

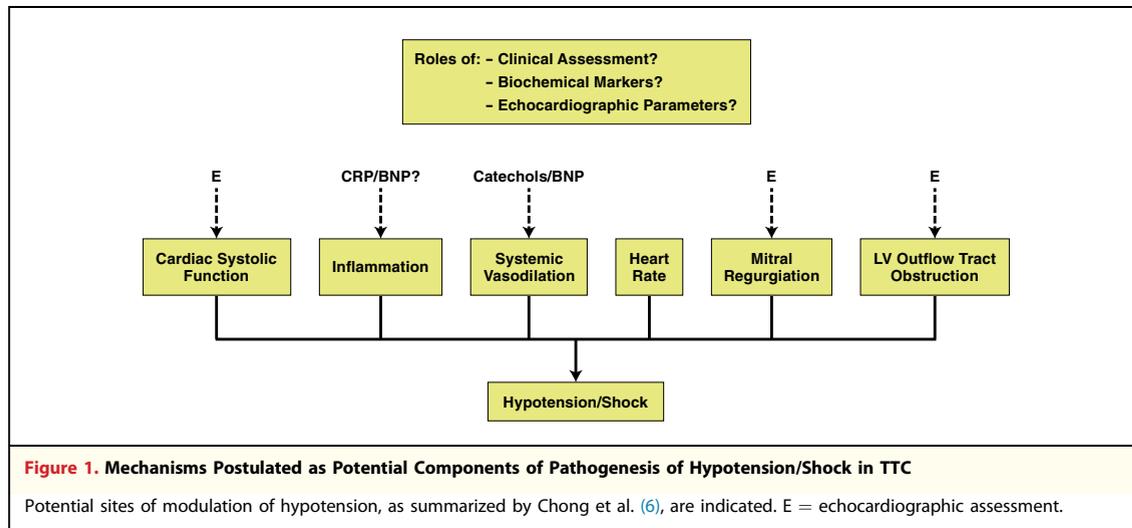
the first 24 h after symptom onset. This may extend to severe shock (6), although interestingly, in most cases, without pulmonary edema. Previous small studies have raised the possibility that severity of TTC episodes and, in particular, the concomitant presence of mitral regurgitation (MR), left ventricular outflow tract obstruction (LVOTO), and extent of right ventricular hypokinesis might contribute to the probability of development of shock (Fig. 1) (7,8). Importantly, the treatment of shock in TTC represents a therapeutic dilemma, as catecholamine administration, in theory, should be avoided. Levosimendan has been suggested (9,10), although to date, clinical data are limited. Also, some patients have been treated via intra-aortic balloon pump insertion. Despite this, there is a significant (perhaps 3%) acute mortality rate associated with TTC, largely due to unresponsive cases of shock.

In this issue of *JACC*, Citro et al. (11) report the results of a collaborative study carried out in 12 Italian centers, evaluating the potential utility of echocardiography in the setting of acute heart failure/shock associated with TTC. A total of 227 TTC patients were studied, of whom 45 developed early heart failure, 18 developed cardiogenic shock, and 4 died of cardiac causes. The data showed that the combination of heart failure/shock/subsequent mortality was associated substantially with the presence of moderate to severe MR (present in 49 patients) and that advanced age (≥ 75 years of age) also correlated strongly with these outcomes. Importantly, MR was also significantly associated with the combination of shock and mortality.

Although the authors suggest that echocardiographic parameters may have prognostic implications in TTC patients, this is, in reality, far from clear cut. Specifically, the occurrence of shock is almost always an early event in TTC, and thus, shock could hardly be said to have been predicted by

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From the Department of Cardiology, The Queen Elizabeth Hospital, Basil Hetzel Institute, The University of Adelaide, Adelaide, Australia. All authors have reported that they have no relationships relevant to the contents of this paper to disclose.



the echocardiographic results; rather, the occurrence of MR can be regarded as a potential contributor to this complication. Interestingly, the precise cause(s) of MR in TTC is uncertain. In the current study, there was no obvious association with LVOTO (which was not commonly seen) or with the extent of LV dyskinesia or major site of LV hypokinesia. In theory, given the recent demonstration of extensive LV inflammation in TTC (4), inflammatory dysfunction of papillary muscles also represents a possible cause. The number of deaths in this study is too small to be used to predict mortality per se.

It should be also emphasized that hypotension/shock after TTC may reflect noncardiac factors such as chronotropic incompetence and paradoxical peripheral vasodilatation (6). Nevertheless, the study by Citro et al. (11) serves to alert us that the presence of significant MR in TTC patients is a substantial contributor to hemodynamic crises in this condition.

Finally, we must resist the temptation to regard the prevention and/or treatment of shock as the only

significant therapeutic challenge in patients with TTC. There is now overwhelming evidence that symptoms resolve slowly, with as many as 50% of patients still symptomatic 2 years after an acute attack (12), that inflammatory activation (4) and BNP release (5) persist for at least 3 months, and that there are subtle but detectable, residual anomalies of left ventricular systolic dysfunction at that stage. Preliminary data (13) have suggested impairment of myocardial energetics in TTC, but the duration of this problem during recovery has not been reported. Moreover, the long-term recurrence rate of TTC is approximately 3% per annum (14).

Thus TTC, as both an acute and subacute disease process, remains very much a work in progress.

Reprint requests and correspondence: Dr. John D. Horowitz, Department of Cardiology, The Queen Elizabeth Hospital, 28 Woodville Road, Woodville South, Adelaide, South Australia 5011. E-mail: john.horowitz@adelaide.edu.au.

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Key Words: acute heart failure ■ cardiogenic shock ■ stress cardiomyopathy ■ tako-tsubo cardiomyopathy.