Takotsubo syndrome has emerged as a unique form of acute myocardial injury associated with chest pain or dyspnea, new ST-T segment abnormalities, serum cardiac enzyme release, distinctive transient regional myocardial dysfunction, and absence of significant coronary disease at coronary angiography. Initially described in 1991 by Sato et al in Japan, Takotsubo syndrome became internationally recognized, with more than 1000 reports by 2011. Although its clinical manifestation usually spontaneously resolves over time, Takotsubo syndrome is not always a disease with a benign course.

When evaluating the pathogenesis of Takotsubo syndrome, it seems that further clinical research is required to gain insight into the causes, triggers, and molecular mechanisms that may be involved. The first description of Takotsubo cardiomyopathy was presented as myocardial stunning due to transient simultaneous multivessel coronary vessel spasm. The frequent association of this syndrome with severe emotional or physical stress supports a neurogenic origin of the disease through increased adrenergic stimulation that directly or indirectly affects cardiac perfusion and function. With the use of invasive and non-invasive imaging techniques, several investigators have presented data indicating a role of microvascular dysfunction in Takotsubo syndrome. Indeed, increased coronary microvascular constriction has been indirectly suggested by the presence of reduced TIMI frame count at urgent coronary angiography with improvement of coronary flow reserve at 1 month.

The initial differential diagnosis of Takotsubo syndrome from acute coronary syndrome (ACS) remains challenging (Table 1). The prevalence of Takotsubo syndrome among patients presenting with ACS is reported to range between 1.2% and 2.0%. Although previous studies have indicated that the disease occurs exclusively in postmenopausal women, being often associated with emotional or physical stress, the absence of these features does not preclude the diagnosis of the disorder. Moreover, electrocardiographic changes and cardiac enzymes or BNP elevation on admission may not always be sufficient to differentiate between these two disorders. Most importantly, the presence of coronary artery disease is not an exclusion criterion for the diagnosis of the disorder. It seems that definitive diagnosis of the syndrome is only substantiated by the normalization of myocardial dysfunction at follow-up. Cardiac magnetic resonance may also be considered in the differential diagnosis not only in the acute phase but also during the follow-up, mostly in patients who do not show wall motion abnormality recovery (Figure 1).

Although Takotsubo syndrome has been considered a benign condition, it seems to carry a small but important risk for adverse outcomes. Hemodynamic instability and cardiogenic shock requiring intervention with vasopressor drugs or intra-aortic balloon pump occurs in 15%, and inhospital mortality in 3–5%. Despite complete and often rapid cardiac recovery, posthospital survival may be less than that in the general population of the same age and is similar to patients hospitalized for acute myocardial infarction, largely because of concomitant illnesses. A recurrence rate of 5–10% has also been reported.

The study by Glaveckaité et al. published in this issue of Hellenic Journal of Cardiology represents a comprehensive retrospective analysis of patients diagnosed with Takotsubo syndrome. The authors add important information to previous evidence on the presenting patterns, clinical course, and mid-term outcome of this syndrome. In line with previous studies, this study showed an uneven gender distribution of the disease, with most of the patients indeed being postmenopausal women. Interestingly, however, approximately half of the patients showed no physical or emotional triggers. Most of the patients presented with chest pain (64%) and new electrocardiographic changes (80%); 5% of the patients had non-significant coronary artery disease, whereas the remainder had normal coronary arteries. Most importantly and in line with recent studies, this study illustrates the previously underestimated risk of complications during the acute phase of the disease and highlights the need for concise clinical evaluation, monitoring, and management.

The in-hospital mortality in this study was 8%, and the rate of cardiogenic shock was 23%. Interestingly, the only significant predictor of in-hospital mortality was the presence of reduced TIMI frame count at urgent coronary angiography. The initial differential diagnosis of Takotsubo syndrome among patients presenting with ACS is reported to range between 1.2% and 2.0%. Although previous studies have indicated that the disease occurs exclusively in postmenopausal women, being often associated with emotional or physical stress, the absence of these features does not preclude the diagnosis of the disorder. Moreover, electrocardiographic changes and cardiac enzymes or BNP elevation on admission may not always be sufficient to differentiate between these two disorders. Most importantly, the presence of coronary artery disease is not an exclusion criterion for the diagnosis of the disorder. It seems that definitive diagnosis of the syndrome is only substantiated by the normalization of myocardial dysfunction at follow-up. Cardiac magnetic resonance may also be considered in the differential diagnosis not only in the acute phase but also during the follow-up, mostly in patients who do not show wall motion abnormality recovery (Figure 1).

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mortality was peak troponin I levels, although it is known that there is no correlation between troponin levels and the extent of myocardial damage in Takotsubo syndrome. The overall survival was 83%, representing a mortality rate of 17.2% at a mean of 3 years follow-up. Significant predictors of overall survival were BNP elevation and cardiogenic shock on admission. This study, as acknowledged by the authors, is limited by its retrospective nature. Future prospective studies may validate the findings of Glaveckaite et al., who reported herewith and shed additional light on the prognostication and outcome of Takotsubo syndrome. Treatment approaches for this disorder may also need customization based on these factors, with a subset of patients clearly needing more intensive monitoring and management.

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### References


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Figure 1 Diagnostic algorithm of Takotsubo syndrome. ACS: Acute coronary syndrome, CAD: Coronary Artery Disease, ECG: Electrocardiogram, TTS: Takotsubo Syndrome, WMA: Wall Motion Abnormality.