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TAKOTSUBO SYNDROME – CURRENT KNOWLEDGE AND CLINICAL CHALLENGES

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ABSTRACT

"Broken heart syndrome" is one of several terms used to describe Takotsubo syndrome. This name refers to the fact that severe emotional or physical stress is considered to be a triggering factor for the disease. Takotsubo syndrome is an acute cardiac condition characterized by reversible ventricular dysfunction and various cardiac wall-motion abnormalities. It presents with a symptom profile that closely resembles acute coronary syndrome. Therefore, it is usually underdiagnosed, especially in patients who have co-existing coronary artery disease. Despite its transient nature, the condition may be associated with various life-threatening complications including arrhythmias, acute heart failure, cardiogenic shock, ventricular thrombus and risk for cerebrovascular events.

Purpose: The aim of this review is to present the current state of knowledge about Takotsubo syndrome and to highlight aspects that require further investigation and systematization.

Materials and Methods: A literature review was conducted from the PubMed database, covering studies from 2015-2025. Key phrases such as "Takotsubo Syndrome", "Broken Heart Syndrome", "Stress Cardiomyopathy" were used. Selected papers were analyzed and evaluated for conclusions.

Conclusions: Takotsubo syndrome remains incompletely understood, with significant gaps in its diagnostic criteria, therapeutic management, and strategies for preventing recurrence. Further research, including large-scale clinical trials and comprehensive meta-analyses, is essential to establish evidence-based guidelines and improve patient outcomes.

KEYWORDS

Takotsubo Syndrome, Broken Heart Syndrome, Stress Cardiomyopathy, Acute Coronary Syndrome

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Introduction

Takotsubo syndrome (TTS) can be found in medical publications under various names including "Broken Heart Syndrome", "Stress Cardiomyopathy" and "Apical Ballooning Syndrome". The disease is an acute cardiac condition characterized by reversible ventricular dysfunction and cardiac wall-motion abnormalities, usually triggered by severe emotional or physical stress. This aspect is reflected in some of the mentioned terminology.

Takotsubo syndrome was first described in Japan in 1990 by the physician Hikaru Sato. The etymology of the word "Takotsubo" derives from the characteristic appearance of the left ventricle at end-systole on cardiac ventriculogram, resembling the traditional Japanese octopus trap. The shape of the vessel with a narrow neck and round bottom prevents exit once the octopus enters. [1]

The clinical presentation of the condition most commonly mimics acute coronary syndrome, not only in relation to the symptom profile but also due to characteristic electrocardiographic changes and elevated cardiac biomarker levels. A distinguishing feature between these two syndromes is usually the absence of significant coronary artery obstructions and the reversible nature of the ventricular wall motion abnormalities. However, the strong similarity between them makes Takotsubo syndrome usually underdiagnosed, especially in patients who have co-existing coronary artery disease. [1][2]

Although more than three decades have elapsed since the condition was first described, its pathophysiological mechanisms remain incompletely understood. It is considered that excessive catecholamine release, coronary microvascular dysfunction, and disturbances in the brain-heart axis play a contributory role in the development of the syndrome. [3][5][7][8]

Despite its transient nature, Takotsubo syndrome may be associated with various life-threatening complications including arrhythmias, acute heart failure, cardiogenic shock, ventricular thrombus and risk for cerebrovascular events. Therefore, the absence of standardized treatment guidelines and the potential for recurrence highlight the need for a deeper understanding of this unique cardiac condition. [3][7][10]

Epidemiology

Takotsubo syndrome accounts for approximately 1–3% of all patients presenting with symptoms suggestive of acute coronary syndrome and 5–6 % of suspected ST-segment elevation myocardial infarctions (STEMI) in women. However, its true prevalence is likely underestimated. Around 90% of Takotsubo syndrome cases occur in postmenopausal women, with a peak incidence around the age of 70. Women appear to be more susceptible than men to developing the syndrome in response to emotional stressors.

Approximately one-third of all patients report an emotional trigger, another third report a physical trigger, while the remaining third present without any identifiable precipitating factor for their Takotsubo syndrome episode. Nearly 10% of patients announce a combination of both emotional and physical stressors. Stressful triggering events are reported in about 89% of cases within the 12 hours preceding a Takotsubo syndrome episode. [2][3]

Pathophysiology

Although more than three decades have elapsed since Takotsubo syndrome was first described, its pathophysiological mechanisms remain incompletely understood. Considering the association of the syndrome with physical or emotional stress, exaggerated responses to triggers by the central and autonomic nervous systems and other stress-related physiological pathways, including the hypothalamic-pituitary-adrenal axis are regarded as a potential key mechanism. In particular, catecholamines such as epinephrine and norepinephrine, which are released during times of stress. Evidence suggests that during the acute phase, the massive direct release of catecholamines from sympathetic nerve endings into the myocardium leads to ventricular dysfunction. It is considered that this local catecholamine excess dysregulates myocardium and has more cardiotoxic effects than the circulating one. This localized catecholamine overexpression may also account for the fact that circulating catecholamine levels are not always elevated and conditions such as pheochromocytoma, which results in massively elevated catecholamine levels in the bloodstream, rarely provoke Takotsubo syndrome.

The effect of catecholamines on the myocardium is modulated by the local distribution and density of adrenergic receptors. β1-adrenergic receptors, which are predominantly located in the basal segments, primarily respond to norepinephrine and mediate positive inotropic effects. In contrast, β2-adrenergic receptors are more densely expressed in the apical segments and in response to epinephrine mediate a negative inotropic effect, contributing to the apical hypokinesis characteristic of Takotsubo cardiomyopathy.

However, current evidence is insufficient to definitively confirm this pathophysiological mechanism. Moreover, the existence of other anatomical variants and the occurrence of Takotsubo syndrome in the absence of an identifiable stressor suggest that the underlying processes are more complex and remain poorly understood. [3][5][7][8]

Over the past two decades, the association between Takotsubo syndrome and acute coronary microvascular dysfunction has been intensively studied as another potential key mechanism in the pathogenesis of the syndrome. Studies suggest that both mechanisms contribute to the development of Takotsubo syndrome, and that coronary microvascular spasm may represent the final common pathway leading to Takotsubo syndrome. Based on these findings, Takotsubo syndrome may be considered an acute coronary microangiopathic syndrome, further supporting the hypothesis of classifying it within the spectrum of acute coronary syndromes. [1][3][5]

Moreover, evidence suggests that individual susceptibility plays a role in the development of Takotsubo syndrome.

According to the observation that the majority of Takotsubo syndrome cases occur in postmenopausal women, estrogen deficiency has been proposed as a potential pathogenetic mechanism. Estrogens provide multifaceted cardiovascular protection, primarily by modulating serum lipid profiles, regulating coagulation pathways, and maintaining endothelial integrity. Furthermore, estrogens critically influence autonomic nervous system regulation. The decline in estrogen levels after menopause may therefore predispose individuals to Takotsubo syndrome, especially forms triggered by emotional stress, through both direct effects on myocardial and coronary vascular function and the loss of estrogen's modulatory and protective influence on neural control mechanisms. However, the available research on this topic remains inconclusive. [1][5]

The idea of a genetic predisposition to Takotsubo syndrome has been suggested based on observations of both individual vulnerability to developing or recurring episodes, as well as cases occurring within the same family. However, studies aimed at confirming this theory have shown mixed results. Since increased adrenergic activity is a common feature in patients with Takotsubo syndrome, most research has focused on

genes related to the adrenergic system. Some smaller studies have also looked into genetic variants linked to estrogen receptors and oxidative stress mediators, but more data from larger studies are needed to draw firm conclusions. [5][7]

Putting together the mentioned processes, studies suggest the following potential pathophysiological mechanism. Takotsubo syndrome is triggered by a precipitating factor such as a physically or emotionally stressful event, pheochromocytoma, acute brain disorders, or certain medications acting on a susceptible individual. This susceptibility may include estrogen deficiency, limbic system alterations, genetic and epigenetic factors, and underlying inflammatory conditions, all of which contribute to sympathetic hyperactivity. As a consequence, acute coronary microvascular spasm occurs, leading to myocardial dysfunction. This proposed mechanism would explain the restoration of cardiac function in over 80% of cases, as microvascular spasm activates the same survival pathways as myocardial hibernation, thereby preventing cardiomyocyte necrosis and subsequent myocardial scarring. [1][3][5]

Anatomical Variants

Takotsubo syndrome presents in several anatomical variants, each defined by the distribution of wall motion abnormalities in the left and sometimes right ventricle.

The most common form is the classic (apical) variant, accounting for approximately 75–80% of cases. It is characterized by hypokinesia or akinesia of the apical segments of the left ventricle, while the basal segments remain hyperkinetic. This pattern creates the typical "octopus trap" appearance, from which the condition gets its name.

The inverted (basal) variant is seen in around 2-3% of patients. In this form, the basal segments are hypokinetic, whereas the apex demonstrates preserved or enhanced contractility. It is more frequently observed in younger individuals and may be triggered by a catecholamine surge, such as from a pheochromocytoma or drug use.

The mid-ventricular variant, responsible for about 10–20% of cases, involves the middle segments of the left ventricle. Both the apex and the base maintain normal function. This pattern may be associated with dynamic left ventricular outflow tract obstruction.

The focal variant is rare, occurring in less than 1% of cases. It involves hypokinesia of a single segment of the left ventricle, with preserved contractility elsewhere. Because of its localized nature, this form may be mistaken for myocardial infarction or myocarditis. Therefore careful differential diagnosis is necessary.

The biventricular variant is extremely rare and involves both the left and right ventricles, leading to global ventricular dysfunction. It is associated with more severe clinical presentations and a higher risk of complications.

Understanding these anatomical variants is crucial for accurate diagnosis, risk stratification, and management of patients with Takotsubo syndrome. Advanced imaging modalities, including echocardiography and cardiac MRI, play a pivotal role in differentiating these variants and guiding appropriate therapeutic strategies. [4][11][12][13]

Clinical Presentation

Takotsubo syndrome is classified as either primary or secondary based on clinical presentation and context.

In primary TTS, patients typically present with acute cardiac symptoms that prompt immediate medical attention. The most commonly reported symptom is chest pain, occurring in over 75% of cases, followed by dyspnea in approximately 50% of patients, and dizziness in more than 25%. Other manifestations may include generalized weakness and, less frequently, syncope. Electrocardiographic findings often mimic those seen in acute coronary syndrome and may include ST-segment elevation or depression, QT interval prolongation, and T wave inversion. Cardiac biomarkers such as troponin T or I, creatine kinase-MB, and B-type natriuretic peptide (BNP) are typically elevated. Nearly all patients undergo coronary angiography, which usually reveals clear coronary arteries or obstructive coronary artery disease that does not correspond with the regional wall motion abnormalities. However, coexisting coronary artery disease is observed in approximately 15% of cases. While some presentations may be idiopathic, primary Takotsubo syndrome is frequently precipitated by emotional or psychological stress, hence its colloquial name: "broken heart syndrome." Taken together, the symptoms, ECG changes, and biomarker elevations closely resemble those of acute coronary syndrome, often making initial differentiation challenging.

In contrast, secondary TTS develops as a complication in patients already hospitalized for an acute medical or surgical condition. It is most often associated with critical illness, trauma, or physiological stress. Conditions commonly linked to secondary TTS include acute exacerbation of asthma or chronic obstructive pulmonary disease, pneumonia, pulmonary embolism, sepsis, subarachnoid hemorrhage, traumatic brain or spinal injury, epileptic seizures, pheochromocytoma, thyrotoxicosisand, acute anxiety, suicide attempt, or drug withdrawal syndrome. [1][2][10]

Diagnosis

Patients with Takotsubo syndrome are most often initially diagnosed with acute coronary syndrome during their first contact with healthcare services due to the very similar clinical presentation. The primary diagnostic test performed is electrocardiography. Abnormalities such as ST-segment elevation or depression, prolonged QT interval, and T wave inversion are observed in the both conditions, as well as cardiac biomarker levels elevation. In order to distinguish between these two conditions during the acute phase, before coronary angiography is performed, the InterTAK Diagnostic Score was established as a clinical assessment tool. It includes seven clinical parameters and can be easily applied in the emergency room. According to its authors, the score demonstrates high sensitivity and specificity. The point distribution is as follows: female sex – 25 points, emotional trigger – 24, physical trigger – 13, absence of ST-segment depression – 12, psychiatric disorders – 11, neurologic disorders – 9, and QTc prolongation – 6. The maximum possible score is 100 points. According to the research a score of ≥ 50 was associated with a 95% accuracy in diagnosing Takotsubo syndrome. Conversely, a score of ≤ 31 predicted acute coronary syndrome with the same accuracy. The InterTAK Diagnostic Score can help avoid unnecessary invasive diagnostic procedures, especially in patients without ST-segment elevation on electrocardiogram. However, in practice almost all takotsubo cardiomyopathy patients undergo coronary angiography. The procedure usually reveals clear coronary arteries or obstructive coronary artery disease that does not correspond with the regional wall motion abnormalities. But coexisting coronary artery disease does not exclude the diagnosis and is observed in approximately 15% of cases. [10][14]

The first diagnostic criteria for Takotsubo cardiomyopathy were introduced in 2003 and further refined a year later by cardiologists from the Mayo Clinic. According to the standardized criteria they proposed, the following four conditions had to be met in order to establish the diagnosis. First, the presence of left ventricular wall motion abnormalities in the form of akinesia or dyskinesia involving the mid-ventricular segments and the apex, or without the apex. Second, the absence of significant stenosis in the coronary arteries and no angiographic evidence of plaque rupture on coronary angiography. Third, the presence of electrocardiographic changes suggestive of myocardial ischemia, such as ST-segment elevation and/or negative T waves and/or elevated cardiac necrosis markers. Fourth, the absence of conditions that could present with a similar echocardiographic appearance, such as myocarditis, hypertrophic cardiomyopathy, or pheochromocytoma.

These criteria remained in use until 2018, when experts from the European Society of Cardiology (ESC) published a consensus document that clarified the clinical presentation, diagnostic criteria, and pathophysiology of Takotsubo syndrome. In this document, they introduced the following international diagnostic criteria known as the InterTAK Diagnostic Criteria. The criteria includes the following points:

- Transient left ventricular dysfunction (hypokinesia, akinesia, or dyskinesia) presenting as apical ballooning or involving midventricular or basal segments, or other patterns of regional wall motion abnormalities; right ventricular involvement may also be present. These regional wall motion abnormalities typically extend beyond the distribution of a single epicardial coronary artery, although such a presentation cannot be completely ruled out.
- Exposure to a physical, emotional, or combined trigger often precedes the onset of symptoms, but is not required for diagnosis.
- Neurological disorders (e.g., intracerebral hemorrhage, TIA, stroke, or syncope) or pheochromocytoma may act as precipitating factors.
- New electrocardiographic abnormalities such as ST-segment elevation or depression, T wave inversion, or QTc interval prolongation; however, ECG changes may be absent in some cases.
- Moderate elevation of cardiac biomarkers, including troponins and CK-MB, is common. BNP levels are often markedly elevated.
- Presence of significant coronary artery disease does not rule out a diagnosis of Takotsubo syndrome.
- Absence of evidence for myocarditis (cardiac MRI is recommended to exclude it).
- Predominantly affects postmenopausal women.

Despite attempts to standardize diagnostic criteria, in the field of cardiology Takotsubo syndrome remains one of the most underdiagnosed conditions in clinical practice. Among the diagnostic challenges contributing to this fact, several key factors can be identified.

Firstly, TTS can be masked by various clinical conditions, especially when it arises as a complication secondary to physical stressors such as acute neurological disorders or sepsis. For this reason, physicians should regularly monitor cardiac biomarkers and ECG changes, and, when necessary, perform cardiac imaging at regular intervals, particularly in critically ill patients who may be at risk of developing Takotsubo syndrome. Additionally, various pre-existing cardiac conditions such as hypertrophic cardiomyopathy with apical aneurysm can potentially mask the onset of a Takotsubo syndrome episode. Secondly, some forms of Takotsubo syndrome may be mild or completely asymptomatic, which can result in patients not seeking medical attention. Thirdly, TTS can sometimes present with focal or extensive wall motion abnormalities involving the entire left ventricle or even both ventricles, which contribiute to an additional diagnostic challenge. The reason is that these anatomical variants, especially the focal one, are more commonly associated with conditions such as acute coronary syndrome (ACS) or myocardial infarction with non-obstructive coronary arteries (MINOCA). Fourthly, the reversible nature of TTS may lead to rapid normalization of wall motion abnormalities before cardiac imaging diagnostic tests are performed. It may contribute to alternative diagnoses including ACSs and MINOCA. [1][7][16]

Treatment

Takotsubo Syndrome (TTS) remains without standardized treatment protocols validated by prospective, randomized controlled trials (RCTs). Nevertheless, a recent consensus statement from an international expert panel on TTS provides evidence-based recommendations aimed at optimizing clinical management[11]. Continuous electrocardiographic monitoring is critical, as QT interval prolongation may predispose patients to life-threatening ventricular arrhythmias, including torsades de pointes, and may also be associated with high-grade atrioventricular (AV) block.[17] Management of patients presenting with cardiogenic shock or post-resuscitation status requires intensive care support, with therapeutic strategies individualized based on the presence of pulmonary edema, severely reduced left ventricular ejection fraction (LVEF), hypotension, and bradycardia. Importantly, the use of inotropic agents is contraindicated due to the potential exacerbation of dynamic left ventricular outflow tract obstruction and arrhythmogenic risk. Retrospective cohort studies and meta-analyses have indicated a potential benefit from the use of angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs), demonstrating associations with improved survival outcomes and decreased recurrence rates of TTS.[24] Given emerging evidence suggesting a central role of systemic and myocardial inflammation in the pathophysiology and prognosis of TTS, the investigation of anti-inflammatory therapeutic strategies warrants further exploration. However, prospective, randomized trials specifically addressing anti-inflammatory interventions in well-defined TTS populations remain a critical unmet need**.**[19][21]

Risk Stratification

Risk stratification in Takotsubo syndrome (TTS) is challenging due to its heterogeneous clinical presentation and pathophysiology.

Among the currently available tools, the InterTAK prognostic score appears to be the most validated method for assessing both short- and long-term mortality risk. [9] This scoring system assigns specific point values to individual clinical variables as follows: Intertak class IIB (15 points), Intertak class IIa (9 points), age>70 (8 points), SBP <119 mmHG on admission (7 points), Diabetes mellitus (6 points), left ventricular ejection fraction (LVEF) ≤ 45% on admission (6 points), Male sex (6 points), heart rate >94 bpm on admission (4 points), InterTAK Classes III (3 points).

It stratifies patients into four risk groups. Low risk ≤15 points, intermediate risk 16–22 points, high risk 23–28 points, and very high risk ≥29 points. Patients, with higher risk groups demonstrating significantly increased mortality compared to the low-risk group.[25]

Recent studies suggest that elevated C-reactive protein (CRP) levels at discharge serve as an independent predictor of 1-year mortality in patients with TTS. When combined with the InterTAK score, CRP measurement may improve the accuracy of long-term risk prediction.[9]

Additional tools that may aid in risk assessment include echocardiography parameters and the CHA_2DS_2-VASc score, particularly in patients with concomitant atrial fibrillation or high cardiovascular risk. Notably, a reduced mitral annular plane systolic excursion (MAPSE) and a high CHA_2DS_2-VASc score have been associated with increased long-term mortality in TTS patients. [26][27]

Prognostication

Despite its transient nature, Takotsubo syndrome may be associated with various life-threatening complications including arrhythmias, acute heart failure, cardiogenic shock, ventricular thrombus and risk for cerebrovascular events. TTS largely depends on the inciting trigger. Patients with physical such as critical illness, sepsis, trauma, post-surgical state, intracranial hemorrhage, cerebrovascular accident or no identifiable triggers had worse outcomes than those with emotional triggers. It is associated with longer hospital stay and lower ventricular function, with hypoxia-triggered TTS having the highest short- and long-term mortality. Patients with TTS which is caused by physical inciting trigger had also higher incidence of cardiogenic shock, cardiac enzyme levels, increased use of inotropes or mechanical circulatory support, mechanical ventilator dependence, increased TTS recurrence rates, and higher number of cardiovascular events resulting in readmissions. Additionally we notice a variable course depending on the sex. Male sex have worse outcomes compared to their female counterparts in TTS.[22][23]

TTS generally carries a favorable prognosis, the development of cardiogenic shock significantly worsens outcomes, necessitating early risk stratification and intensive monitoring in high-risk populations. [22][23]

Conclusions

Takotsubo syndrome is often referred to in various publications as Takotsubo cardiomyopathy. However, this terminology is now considered inaccurate, as Takotsubo syndrome is, by definition, a transient condition in which myocardial abnormalities typically resolve fully or partially following the acute episode. Furthermore, the pathophysiological mechanisms discussed in this paper support the hypothesis that the syndrome belongs within the spectrum of acute coronary syndromes. These factors, among others, contribute to the current consensus among experts that Takotsubo syndrome should not be classified as a cardiomyopathy. [18]

Takotsubo syndrome is a fascinating but still not fully understood phenomenon, as demonstrated in this paper. Despite the growing number of scientific articles in the medical literature, there is still a lack of large-scale clinical studies that could clearly confirm or exclude the proposed mechanisms contributing to the development of this condition. Additionally, despite attempts to standardize diagnostic criteria, Takotsubo syndrome continues to be one of the most underdiagnosed conditions in cardiology in clinical practice. Its resemblance to other cardiac conditions demands heightened clinical awareness and an extensive differential diagnosis that includes both invasive and non-invasive diagnostic tests.

Recent clinical observations and available data indicate that Takotsubo syndrome is a significantly more serious condition than initially presumed. While many patients experience full recovery, a subset faces significant complications, including acute heart failure, arrhythmias, thromboembolism, cardiogenic shock, and even death.Current methods for risk stratification and early identification of patients likely to develop severe manifestations of TTC remain unsatisfactory. Additionally, there are no established universal guidelines for pharmacological management of Takotsubo syndrome (TTS). Treatment is not targeted, it is primarily supportive and tailored to the patient’s condition. Studies have shown that commonly prescribed medications, including beta-blockers and angiotensin-converting enzyme (ACE) inhibitors, do not significantly reduce the risk of relapse or mortality among TTC patients. Randomized clinical trials are necessary to determine optimal pharmacological strategies and long-term outcomes in TTS patients.

Disclosure

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REFERENCES

1. Boyd B, Solh C.Takotsubo cardiomyopathy. Review of broken heart syndrome. JAAPA. 2020;33(3):24-29. https://doi.org/10.1097/01.jaa.0000654368.35241.fc
2. Matta AG, Carrié D. Epidemiology, Pathophysiology, Diagnosis, and Principles of Management of Takotsubo Cardiomyopathy: A Review. Med Sci Monit. 2023;29:93020. https://doi.org/10.12659/msm.939020
3. von Känel R, Usseglio J, Rojas DA, David ML, Khan I, Goyal P, Edmondson D, Kronish IM, Birk JL. Peripheral physiologic responses to acute psychological stress in Takotsubo syndrome: A systematic review and meta-analysis. Neurosci Biobehav Rev. 2025 May:172:106129. https://doi.org/10.1016/j.neubiorev.2025.106129
4. Templin C, Ghadri JR, Diekmann J, Napp LC, Bataiosu DR, Jaguszewski M, Cammann VL, Sarcon A, Geyer V, Neumann CA, Seifert B, Hellermann J, Schwyzer M, Eisenhardt K, Jenewein J, Franke J, Katus HA, Burgdorf C, Schunkert H, Moeller C, Thiele H, Bauersachs J, Tschöpe C, Schultheiss HP, Laney CA, Rajan L, Michels G, Pfister R, Ukena C, Böhm M, Erbel R, Cuneo A, Kuck KH, Jacobshagen C, Hasenfuss G, Karakas M, Koenig W, Rottbauer W, Said SM, Braun-Dullaeus RC, Cuculi F, Banning A, Fischer TA, Vasankari T, Airaksinen KE, Fijalkowski M, Rynkiewicz A, Pawlak M, Opolski G, Dworakowski R, MacCarthy P, Kaiser C, Osswald S, Galiuto L, Crea F, Dichtl W, Franz WM, Empen K, Felix SB, Delmas C, Lairez O, Erne P, Bax JJ, Ford I, Ruschitzka F, Prasad A, Lüscher TF.. Clinical Features and Outcomes of Takotsubo (Stress) Cardiomyopathy. N Engl J Med. 2015;373(10):929-938. https://doi.org/10.1056/nejmoa1406761
5. Crea F, Iannaccone G, La Vecchia G, Montone RA. An update on the mechanisms of Takotsubo syndrome: "At the end an acute coronary syndrome" J Mol Cell Cardiol. 2024 Jun;191:1-6. https://doi.org/10.1016/j.yjmcc.2024.04.009
6. Yalta K, Madias JE, Kounis NG, Y-Hassan S, Polovina M, Altay S, Mebazaa A, Yilmaz MB, Lopatin Y, Mamas MA, Gil RJ, Thamman R, Almaghraby A, Bozkurt B, Bajraktari G, Fink T, Traykov V, Manzo-Silberman S, Mirzoyev U, Sokolovic S, Kipiani ZV, Linde C, Seferovic PM. Takotsubo Syndrome: An International Expert Consensus Report on Practical Challenges and Specific Conditions (Part-2: Specific Entities, Risk Stratification and Challenges After Recovery) Balkan Med J. 2024 Oct 31;41(6):442-457. https://doi.org/10.4274/balkanmedj.galenos.2024.2024-9-99
7. Yalta K, Madias JE, Kounis NG, Y-Hassan S, Polovina M, Altay S, Mebazaa A, Yilmaz MB, Lopatin Y, Mamas MA, Gil RJ, Thamman R, Almaghraby A, Bozkurt B, Bajraktari G, Fink T, Traykov V, Manzo-Silberman S, Mirzoyev U, Sokolovic S, Kipiani ZV, Linde C, Seferovic PM. Takotsubo Syndrome: An International Expert Consensus Report on Practical Challenges and Specific Conditions (Part-1: Diagnostic and Therapeutic Challenges) Balkan Med J. 2024 Oct 31;41(6):421–441. https://doi.org/10.4274/balkanmedj.galenos.2024.2024-9-98
8. Ekenbäck C, Persson J, Tornvall P, Forsberg L, Spaak J. Sympathetic nerve activity and response to physiological stress in Takotsubo syndrome. Clin Auton Res. 2025 Apr;35(2):205-214. https://doi.org/10.1007/s10286-024-01082-9
9. Faucher L, Matsushita K, Kikuchi S, Tatarcheh T, Marchandot B, Granier A, Amissi S, Trimaille A, Jesel L, Ohlmann P, Hibi K, Schini-Kerth V, Morel O. Mortality risk stratification for Takotsubo syndrome: Evaluating CRP measurement alongside the InterTAK prognostic score. ESC Heart Fail. 2025 Jan 16;12(2):1427–1436. https://doi.org/10.1002/ehf2.15161
10. Tantillo S, Guarnera M, Benvenuti F, Ottaviani I, Cilloni N. A Case of Takotsubo Syndrome in a Smoker-Epileptic Patient With Rhinovirus Pneumonia in the Intensive Care Unit: Could the InterTAK Criteria Be Useful? Cureus. 2024 Sep 18;16(9):e69638. https://doi.org/10.7759/cureus.69638
11. Ghadri JR, Wittstein IS, Prasad A, Sharkey S, Dote K, Akashi YJ, Cammann VL, Crea F, Galiuto L, Desmet W, Yoshida T, Manfredini R, Eitel I, Kosuge M, Nef HM, Deshmukh A, Lerman A, Bossone E, Citro R, Ueyama T, Corrado D, Kurisu S, Ruschitzka F, Winchester D, Lyon AR, Omerovic E, Bax JJ, Meimoun P, Tarantini G, Rihal C, Y-Hassan S, Migliore F, Horowitz JD, Shimokawa H, Lüscher TF, Templin C.. International Expert Consensus Document on Takotsubo Syndrome (Part I): Clinical Characteristics, Diagnostic Criteria, and Pathophysiology. Eur Heart J. 2018;39(22):2032-2046. https://doi.org/10.1093/eurheartj/ehy076
12. Lyon AR, Bossone E, Schneider B, Sechtem U, Citro R, Underwood SR, Sheppard MN, Figtree GA, Parodi G, Akashi YJ, Ruschitzka F, Filippatos G, Mebazaa A, Omerovic E.. Current state of knowledge on Takotsubo syndrome: A position statement from the Heart Failure Association of the ESC. Eur J Heart Fail. 2016;18(1):8-27. https://doi.org/10.1002/ejhf.424
13. Medina de Chazal H, Del Buono MG, Keyser-Marcus L, Ma L, Moeller FG, Berrocal D, Abbate A. Stress cardiomyopathy diagnosis and treatment: JACC state-of-the-art review. J Am Coll Cardiol. 2018;72(16):1955-1971. https://doi.org/10.1016/j.jacc.2018.07.072
14. Samul-Jastrzębska J, Roik M, Wretowski D, Łabyk A, Ślubowska A, Bizoń A, Paczyńska M, Kurnicka K, Pruszczyk P, Ciurzyński M. Evaluation of the InterTAK Diagnostic Score in differentiating Takotsubo syndrome from acute coronary syndrome. A single center experience. Cardiology Journal. 2021;28(3):416–422. https://doi.org/10.5603/cj.a2019.0086

15. Kato K, Di Vece D, Kitagawa M, Yamamoto K, Miyakoda K, Aoki S, Goto H, Kitahara H, Kobayashi Y, Templin C. Clinical characteristics and outcomes in takotsubo syndrome -Review of insights from the InterTAK Registry. J Cardiol. 2025 Apr;85(4):263-267. https://doi.org/10.1016/j.jjcc.2025.01.009
16. Waqar A, Jain A, Joseph C, Srivastava K, Ochuba O, Alkayyali T, Poudel S. Cardioprotective Role of Estrogen in Takotsubo Cardiomyopathy. Cureus. 2022 Mar 4;14(3):e22845. https://doi.org/10.7759/cureus.22845
17. Potu KC, Raizada A, Gedela M, Stys A. Takotsubo Cardiomyopathy (Broken-Heart Syndrome): A Short Review. S D Med. 2016 Apr;69(4):169-71.
18. Arbelo E, Protonotarios A, Gimeno JR, Arbustini E, Barriales-Villa R, Basso C, Bezzina CR, Biagini E, Blom NA, de Boer RA, De Winter T, Elliott PM, Flather M, Garcia-Pavia P, Haugaa KH, Ingles J, Jurcut RO, Klaasse S, Limongelli G, Loeys B, Mogensen J, Olivotto I, Pantazis A, Sharma S, Van Tintelen JP, Ware JS, Kaski JP. 2023 ESC Guidelines for the management of cardiomyopathies: Developed by the Task Force on the Management of Cardiomyopathies of the European Society of Cardiology (ESC). Eur Heart J. 2023 Oct 1;44(37):3503–3626. https://doi.org/10.1093/eurheartj/ehad194
19. Singh T, Khan H, Gamble DT, Scally C, Newby DE, Dawson D. Takotsubo Syndrome: Pathophysiology, Emerging Concepts, and Clinical Implications. Circulation. 2022 Mar 29;145(13):1002-1019. https://doi.org/10.1161/circulationaha.121.055854
20. Santoro F, Núñez Gil IJ, Stiermaier T, El-Battrawy I, Guerra F, Novo G, Guastafierro F, Tarantino N, Novo S, Mariano E, Romeo F, Romeo F, Capucci A, Bahlmann E, Zingaro M, Cannone M, Caldarola P, Marchetti MF, Montisci R, Meloni L, Thiele H, Di Biase M, Almendro-Delia M, Sionis A, Akin I, Eitel I, Brunetti ND. Assessment of the German and Italian Stress Cardiomyopathy Score for Risk Stratification for In-hospital Complications in Patients With Takotsubo Syndrome. JAMA Cardiol. 2019 Sep 1;4(9):892-899. https://doi.org/10.1001/jamacardio.2019.2597
21. Pätz T, Santoro F, Cetera R, Ragnatela I, El-Battrawy I, Mezger M, Rawish E, Andrés-Villarreal M, Almendro-Delia M, Martinez-Sellés M, Uribarri A, Pérez-Castellanos A, Guerra F, Novo G, Mariano E, Musumeci MB, Arcari L, Cacciotti L, Montisci R, Akin I, Thiele H, Brunetti ND, Vedia O, Núñez-Gil IJ, Eitel I, Stiermaier T. Trigger-Associated Clinical Implications and Outcomes in Takotsubo Syndrome: Results From the Multicenter GEIST Registry. J Am Heart Assoc. 2023 Jul 18;12(14):e028511. https://doi.org/10.1161/jaha.122.028511
22. Muhammad H, Bag A, Iyer A. Takotsubo Syndrome: Is It Just a "Broken Heart"? J Community Hosp Intern Med Perspect. 2023 Nov 4;13(6):132-133. https://doi.org/10.55729/2000-9666.1262
23. La Vecchia G, Del Buono MG, Sanna T, Capecchi PL, Lazzerini PE, Golino M, Kron J, Rodriguez-Miguelez P, Pelargonio G, Abbate A. Life-Threatening Arrhythmias in Patients With Takotsubo Syndrome: Insights Into Pathophysiology and Treatment Innovations. JACC Clin Electrophysiol. 2024 Aug;10(8):1943-1952. https://doi.org/10.1016/j.jacep.2024.03.034
24. Kim JH, Sunkara A, Varnado S. Management of Cardiogenic Shock in a Cardiac Intensive Care Unit. Methodist Debakey Cardiovasc J. 2020 Jan-Mar;16(1):36-42. https://doi.org/10.14797/mdcj-16-1-36
25. Kato K, Di Vece D, Kitagawa M, Yamamoto K, Miyakoda K, Aoki S, Goto H, Kitahara H, Kobayashi Y, Templin C. Clinical characteristics and outcomes in takotsubo syndrome -Review of insights from the InterTAK Registry. J Cardiol. 2025 Apr;85(4):263-267. Epub 2025 Jan 30. https://doi.org/10.1016/j.jjcc.2025.01.009
26. Parodi G, Scudiero F, Citro R, Silverio A, Bellandi B, Zito C, Antonini-Canterin F, Rigo F, Zocchi C, Bossone E, Salerno-Uriarte J, Piscione F, Mario CD; Takotsubo Italian Network (TIN). Risk Stratification Using the CHA2DS2-VASc Score in Takotsubo Syndrome: Data From the Takotsubo Italian Network. J Am Heart Assoc. 2017 Sep 14;6(9):e006065. https://doi.org/10.1161/jaha.117.006065
27. El-Battrawy I, Ansari U, Lang S, Fastner C, Zhou X, Borggrefe M, Akin I. Risk stratification in Takotsubo syndrome: a role of mitral annular plane systolic excursion. QJM. 2018 Apr 1;111(4):231-236. https://doi.org/10.1093/qjmed/hcy003