

## Takotsubo Cardiomyopathy- Case Report

Howard B Reinfeld\*

### Abstract

A short-term and temporary kind of heart condition is known as Takotsubo Cardiomyopathy. It is triggered by physical or emotional stress and is known as stress-induced cardiomyopathy. A patient with Takotsubo also known as TCM experiences trouble pumping and the heart enlarges. Complications may occur in rare cases, although a 1-month recovery is more often.

**Keywords:** Takotsubo cardiomyopathy; Catecholamine-induced theory; Risk factors.

### Introduction

The heart contains four chambers in which two small atriums are located on the top of the heart, and two larger ventricles are located below the atria. These ventricles functions as the primary pump of the heart. Takotsubo cardiomyopathy is basically a heart disease characterized by the left ventricle ballooning and transient dysfunction accompanied by physical or emotional stress. Takotsubo cardiomyopathy was identified and named in the 1990s in Japan, where Takotsubo word indicates a pot with a narrow neck in Japanese. Its shape is similar to the affected individuals' hearts.

Takotsubo cardiomyopathy's symptoms are similar to heart attack symptoms, including

\*Cardiology Graduate of Mount Sinai Hospital Miami Beach Florida and Cardiologist at Private Practice, Howard B Reinfeld and Associates MD, PA and BS Pharmacy, St. John's University, Jamaica, New York, USA

\*Corresponding Author: Howard B Reinfeld, Cardiology Graduate of Mount Sinai Hospital Miami Beach Florida and Cardiologist at Private Practice, Howard B Reinfeld and Associates MD, PA and BS Pharmacy, St. John's University, Jamaica, New York, USA.

Received Date: 07-25-2022

Accepted Date: 08-05-2022

Published Date: 08-24-2022

Copyright© 2022 by Reinfeld HB. All rights reserved. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

dyspnea (difficult breathing), chest pain, and syncope (loss of consciousness). Symptom control is the fundamental step of its treatment. Usually, it leads to full recovery within a month. Aged women are most affected by this disease as emotional or physical stress triggers it. However, preventive measures may help restrict cardiomyopathy complications [1].

### Causes

Takotsubo cardiomyopathy mechanism is not established properly. However, it was observed that intense emotional stress,

including the death of a closed one, divorce, or bankruptcy contributes to the disease. It is also noticed that physical stress like infection, fracture, or stroke becomes the cause of Takotsubo cardiomyopathy in two to three cases. It was hypothesized that physical and emotional stressors lead to the release of epinephrine (adrenaline) in a large amount. Additionally, it may also release other stress-related hormones, including catecholamine, in large amounts that can lead to TCM. It may cause blood vessel spasms and disrupt ventricles of the heart, which cause ventricular dysfunction and ballooning in cases with TCM.

### Symptoms

It is investigated that Takotsubo cardiomyopathy can be triggered in adults of any age. However, it usually occurs in elderly women. The most common symptoms of TCM include dyspnea, crushing chest pain, diaphoresis, anxiety, palpitations, vomiting, transient loss of consciousness, and nausea. Research shows that patients with TCM are more likely to recover within a month, and the rate of recurrence is not often. However, the studies showed that 20% of patients have the risk of complications.

It was analyzed that patients with TCM are prone to have heart failure as the heart is not able to pump blood efficiently [2]. It may lead to abdomen and leg swelling due to edema. Poor blood pumping may lead to dyspnea and fatigue. In some cases, arrhythmia in which the heartbeat is too slow, too fast, or irregular can occur due to Takotsubo cardiomyopathy. It is observed in some cases that clot formation is also possible in patients with TCM, and these clots may lead to stroke.

However, the chances of these possibilities are minor as 90% of individuals with TCM survive the disease.

### Diagnosis

The studies have shown that patients with Takotsubo cardiomyopathy are more inclined to be considered to have a heart attack until the real cause is proven. Medically, there are two useful and common tests that are done initially in patients with symptoms of acute myocardial infarction. These tests may include an electrocardiogram (ECG), which is used to determine the electrical activity of the heart. It also measures the levels of blood troponin, which is considered a marker of deterioration of the heart. ECG describes the modifications observed in ST-segment elevation myocardial infarction in individuals with TCM. It is the most severe kind of heart attack [3]. ECG also elaborates the troponin levels elevation as they are also in an MI. However, a medical imaging technique, coronary angiography, in which radiographs are used to visualize coronary arteries by injecting dye, is performed where no significant coronary artery occlusion is observed. Ventriculography is used to identify ballooning and ventricular dysfunction, in which a similar principle as coronary angiography is used. However, it enables the visualization of the ventricles instead of coronary arteries. Echocardiography is also used in which ultrasound waves are utilized to visualize the heart more accurately.

Research shows that MRI, cardiac magnetic resonance imaging is also used to diagnose TCM, which is a specialized imaging technique [3]. It is used to evaluate the extent of ballooning and ventricular dysfunction.

According to medical studies, cardiac MRI is one of the most feasible techniques to diagnose Takotsubo cardiomyopathy because it identifies reversible myocardium damage accurately by visually analyzing wall motion abnormalities. Additionally, it assesses fibrosis and inflammation. It is investigated that cardiac MRI is best for the evaluation of left ventricle ejection fraction. It is used to analyze the absence of gadolinium enhancement in individuals with Takotsubo cardiomyopathy. It is observed that this modality is more likely to provide a better perspective on the pathophysiology of TCM. It tends to raise awareness and analyze acute symptoms earlier in order to get better treatments. It also enhances clinical outcomes.

### **Pathophysiology**

Takotsubo cardiomyopathy (TCM) has no exact pathogenesis. However, several hypotheses theories exist in order to discuss pathogenesis, including coronary artery spasm, coronary microvascular dysfunction, catecholamine-induced myocardial stunning, myocardial microinfarction, reperfusion injury following acute coronary syndrome, and cardiac fatty acid metabolism abnormalities. The most supported theories are catecholamine-induced cardiotoxicity and microvasculature dysfunction.

### **Catecholamine-induced theory of TCM**

Research shows that emotional stress plays a significant part and is considered a precipitating factor in patients with TCM, in which serum catecholamine concentration was two to three times more. This comparison is drawn with the myocardial infarction. It is

reported that typical characteristics of TCM are caused by exogenously administered catecholamines which further supports the theory.

Another theory known as stimulus trafficking was explained, which indicated the reduction of myocyte contractile function in patients affected with Takotsubo cardiomyopathy [4]. It has been investigated those higher levels of catecholamines induce  $\beta_2$ -coupling from Gs to Gi. Thus, it is evidenced that the reduction of myocyte contractile functions occurs by hypokinesia in ECG.

In stimulus trafficking rationale, it is suggested that the switch to Gi happens in order to shield myocytes from Gs stronger stimulation which may lead to apoptosis. There is a mild increase in serum troponin level, which describes minimal and early necrosis of the myocardial tissue. Research showed phosphatidyl inositol 3-kinase-protein kinase B (PI3K/AKT) signaling pathway enhanced activity which has a significant anti-apoptosis function. It boosts the quick recovery of myocytes [5]. Therefore, PI3K/AKT pathway and inversely switching from Gi to Gs could be featured by the transient left ventricle dysfunction, which is associated with clinical and rapid recovery of systolic function noticed in TCM.

Microvasculature dysfunction findings are consistently observed in the patients affected with Takotsubo cardiomyopathy. The characteristics investigated of microvasculature dysfunction in patients with TCM include excessive vasoconstriction, abnormality of endothelium-dependent vasodilation, and impairment of myocardial perfusion. Myocardial biopsy observed vast

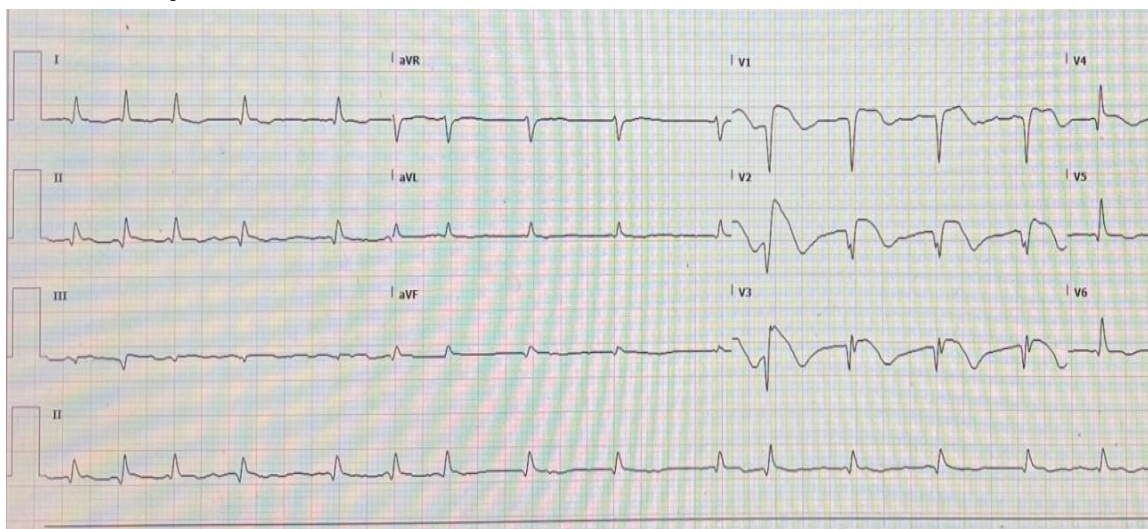
apoptosis in endothelial cells. Another report has investigated the enhanced vulnerability to ergonovine and acetylcholine. It may contribute to transient left ventricle dysfunction as it is similar to vasospastic angina. However, this theory was rejected because the characteristics of vasospasm were shown in just 30% of patients in a challenge test.

Another research has shown that patients with TCM having myocardial biopsy present regions with inflammatory cell infiltration, necrosis, and localized fibrosis. It was evaluated that the higher toxicity levels of catecholamine on cardiac muscle cells cause these modifications. Observation shows that the increase in norepinephrine levels in Takotsubo individuals may lead to an increase in white blood cell counts and C-reactive protein levels. It was also assumed that more systemic inflammation through the induction of proinflammatory cytokine was produced by catecholamines. More observations are yet to be introduced in order

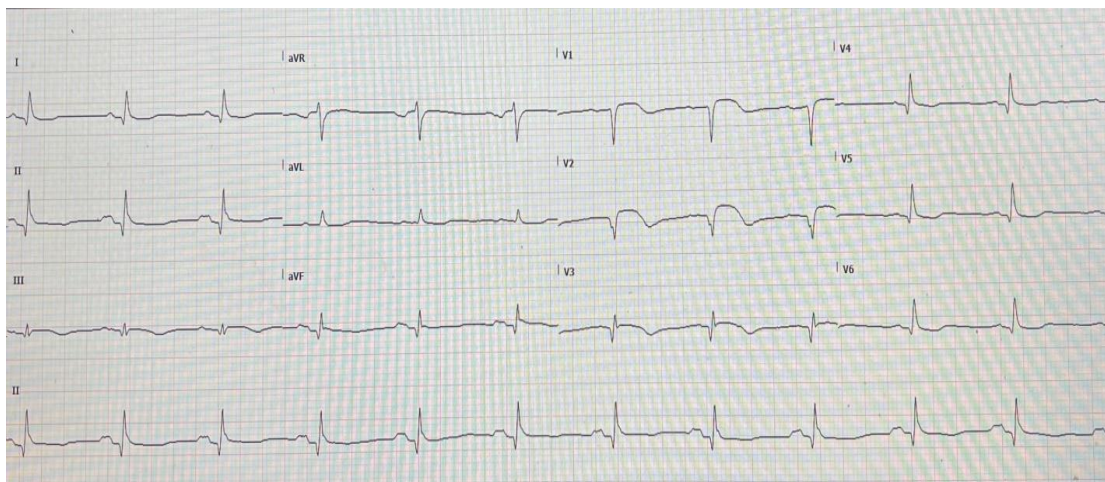
to observe the pathophysiology of TCM accurately [1].

### Case study

95-year-old female arrives to ER with past medical history of Hypertension, Diabetes, with chief complaint of chest pain. EKG on arrival showed acute ST elevation myocardial infarction with atrial fibrillation with rapid ventricular response of 117 bpm and premature complexes. Labs revealed elevated lactic acid. A STEMI Alert was called, and Cardiac Cath was performed. Cath showed no significant occlusion or coronary artery disease on the other hand Echocardiogram showed Antero-apical and infero-apical hypokinesis consistent with stress induced Takotsubo cardiomyopathy. Patient was closely monitored and failed RVR treatment of Metoprolol and Sotalol. Patient was alternatively treated with Amiodarone and converted to sinus rhythm. Figure 1 and 2 show EKGs pre and post treatment. This patient recovered and was discharge home.



**Figure 1:** Pre-treatment EKG.



**Figure 2:** Post-treatment EKG.

### Treatment and management

One thing observed in the cases of Takotsubo cardiomyopathy is that individuals with this disease most recover within a month without even having standard treatment. It has been observed that symptomatic treatment is given to patients with Takotsubo cardiomyopathy during an acute phase.

The studies have shown that there are two classes of medications utilized to provide an enhanced treatment that may improve the survival rate in individuals with TCM [6]. These two classes of medications include angiotensin-receptor blockers (ARB) and angiotensin-converting-enzyme (ACE) inhibitors. These are mainly used to treat high blood pressure. It is observed medically that physicians may prescribe beta-blockers to patients with TCM. Beta-blockers are defined as a class of medication that is used to reduce the activating effects of catecholamines on the heart. However, scientific evidence is lacking in order to prove its improvement in survival in TCM patients [5].

Disease management is mostly relying on the treatment associated with complications and symptom control. Medication that is used to stimulate urine production is given to patients with heart failure risk or occurring heart failure in

order to eliminate excessive fluid. Additionally, vasodilators (medication used to dilate blood vessels) are also prescribed in order to reduce blood pressure in heart failure conditions. People who are more prone to developing cardiogenic shock may require fluid resuscitation. It is investigated that anticoagulants (blood thinners) are administered in some patients with the complication of thrombus (blood clot) formation.

Research shows that emotional and physical stress is highly associated with Takotsubo cardiomyopathy. Therefore, physical and emotional stressors are addressed for the patients with TCM that may contribute to relieving pain and managing TCM symptoms. After normal LV function, a patient is suggested to discontinue drugs [6].

### Risk factors

#### Lack of estrogen

The study shows that postmenopausal women are more likely to be affected by Takotsubo cardiomyopathy. More than 90% of postmenopausal females contain TCM. It was researched to analyze whether hormone replacement therapy works in regard to TCM. The study has shown that no patients with TCM had the tendency to receive estrogen replacement

therapy. It was further demonstrated that LV function decrease was somehow higher in ovariectomized rats subjected to restraint stress than in rats receiving estradiol supplementation. It is investigated that estrogen receptor- $\alpha$  and estrogen receptor- $\beta$  are expressed by myocytes. The transcription of cardioprotective factors, including atrial natriuretic peptide and heat shock protein, is enhanced by estrogen. In response, it gets protection from catecholamines' toxic effect, reduced oxidative stress, and calcium overload.

### Physical or emotional stress inducers

It was reported that people using antidepressants and having depressive disorders are more likely to experience a decrease in vagus nerve tension and increased response to the adrenal medullary hormone. It could be associated with the cause of TCM. It was observed that depressive patients contained a relatively higher amount of noradrenaline extravasation.

### Genetic factors

Research has shown a strong association between polymorphisms of  $\alpha$ - and  $\beta$ -adrenergic receptors and neurogenic stunned myocardium. It emerged as a subarachnoid hemorrhage symptom and showed overlapping pathophysiology with Takotsubo cardiomyopathy. In this regard, there is a higher risk factor associated with genetics.

### Prognosis and recurrence

It is observed that individuals with Takotsubo cardiomyopathy have a good prognosis as almost 96% of cases of TCM are observed as fully recovered. According to studies, around 1 or 2%

mortality rate remains that varies in hospitals [7]. It was thought that TCM would become a benign course. However, around 5% of individuals with TCM have undergone cardiac arrest. They were no different than healthy subjects in terms of long-term survival rate. However, at the time of initial onset, they are more prone to higher mortality risks.

The report shows that chest pain (30%) was one of the most common complications observed. The recurrence of chest pain happened in around 11% of individuals with TCM within 4 years.

The prognostic indicators, signs of thrombolysis in myocardial infarction, ECG findings, N-terminal pro-brain natriuretic peptide level, and grade of myocardial perfusion have been conducted to identify various factors contributing to TCM. However, there was no definite marker observed for the outcome of the disease [8].

### Conclusion

Takotsubo cardiomyopathy is now gaining notice as a significant heart disease seen occurring in all ages but mainly seen in elderly and postmenopausal women. It can be recovered within one month and have a rare chance of recurrence. The symptoms seem to be a heart attack, including arrhythmia, leg swelling, palpitations, nausea, chest pain, and loss of consciousness. It is observed that coronary microvascular dysfunction, coronary spasm, myocarditis, and catecholamine toxicity have a strong association with the pathogenesis of TCM. However, the exact studies are still not understood.

### References

1. Amin HZ, Amin LZ, Pradipta A. Takotsubo Cardiomyopathy: A Brief Review. J Med Life. 2020;13(1):3-7. [PubMed](#) | [CrossRef](#)
2. Roshanzamir S, Showkathali R. Takotsubo cardiomyopathy a short review. Curr Cardiol Rev. 2013;9(3):191-6 [PubMed](#) | [CrossRef](#)
3. Scantlebury DC, Prasad A. Diagnosis of Takotsubo cardiomyopathy. Circ J. 2014;78(9):2129-39. [PubMed](#) | [CrossRef](#)

4. Hurst RT, Prasad A, Askew JW 3rd, Sengupta PP, Tajik AJ. Takotsubo cardiomyopathy: a unique cardiomyopathy with variable ventricular morphology. JACC Cardiovasc Imaging. 2010;3(6):641-9. [PubMed](#) | [CrossRef](#)
5. Komamura K, Fukui M, Iwasaku T, Hirotsu S, Masuyama T. Takotsubo cardiomyopathy: Pathophysiology, diagnosis and treatment. World J Cardiol. 2014;6(7):602-9. [PubMed](#) | [CrossRef](#)
6. Kurisu S, Kihara Y. Clinical management of takotsubo cardiomyopathy. Circ J. 2014;78(7):1559-66. [PubMed](#) | [CrossRef](#)
7. Ono R, Falcão LM. Takotsubo cardiomyopathy systematic review: Pathophysiologic process, clinical presentation and diagnostic approach to Takotsubo cardiomyopathy. Int J Cardiol. 2016; 209:196-205. [PubMed](#) | [CrossRef](#)
8. Yoshikawa T. Takotsubo cardiomyopathy, a new concept of cardiomyopathy: clinical features and pathophysiology. Int J Cardiol. 2015;182:297-303. [PubMed](#) | [CrossRef](#)