

**Takotsubo Cardiomyopathy and its variables: an integrative review***Miocardopatía de Takotsubo y sus variables: una revisión integradora**Miocardopatia de Takotsubo e suas variáveis: uma revisão integrativa***Juliana Mendes Marques<sup>1</sup>**

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**Submission:** 07-30-2021**Approval:** 09-02-2021**Abstract**

In post-modern society, changes in people's lifestyle have triggered both professional and personal problems. In this context, encouraging the biopsychosocial look at the patient, there is a concern to research more about Takotsubo Cardiomyopathy. The objective of this research is to identify studies that address the factors that can trigger Takotsubo myocardiopathy. This is an integrative literature review. The evidence found through the retrieved articles indicates the association of CMT with stressors, this being the most likely variable, it is an underdiagnosed pathology because its findings are confused with Acute Coronary Syndrome. The results of the present study demonstrate the association of stressors with the development of Takotsubo Cardiomyopathy, clarifying possible relationships between them.

**Descriptors:** Takotsubo Cardiomyopathy; Diagnosis; Risk Factor.**Resumén**

En la sociedad posmoderna, los cambios en el estilo de vida de las personas han provocado problemas tanto profesionales como personales. En este contexto, fomentando la mirada biopsicosocial del paciente, existe la preocupación de investigar más sobre la Miocardopatía de Takotsubo. El objetivo de esta investigación es identificar estudios que aborden los factores que pueden desencadenar la miocardopatía de Takotsubo. Ésta es una revisión integradora de la literatura. La evidencia encontrada a través de los artículos recuperados indica la asociación de CMT con factores estresantes, siendo esta la variable más probable, es una patología infradiagnosticada porque sus hallazgos se confunden con el Síndrome Coronario Agudo. Los resultados del presente estudio demuestran la asociación de factores estresantes con el desarrollo de la Miocardopatía de Takotsubo, aclarando posibles relaciones entre ellos.

**Descriptores:** Cardiomiopatía de Takotsubo; Diagnóstico; Factores de Riesgo.**Resumo**

Na sociedade pós-moderna, as mudanças no estilo de vida das pessoas desencadearam problemas tanto profissionais, quanto pessoais. Nesse contexto, incentivando o olhar biopsicossocial para o paciente, surge a inquietação de se pesquisar mais sobre a Cardiomiopatía de Takotsubo. O objetivo dessa pesquisa é identificar estudos que abordem os fatores que podem desencadear a mio cardiopatia de Takotsubo. Trata-se de uma revisão integrativa da literatura. As evidências encontradas através dos artigos recuperados indicam a associação da CMT com fatores estressores, sendo essa a variável mais provável, é uma patologia sub diagnosticada pois seus achados se confundem com a Síndrome Coronariana Aguda. Os resultados do presente estudo demonstram a associação dos fatores estressores com o desenvolvimento da Cardiomiopatia de Takotsubo esclarecendo possíveis relações entre eles.

**Desritores:** Cardiomiopatia de Takotsubo; Diagnóstico; Fatores de Risco.

## Introduction

In postmodern society, changes in people's lifestyle have triggered both professional and personal problems<sup>1</sup>. Emotional disturbances seem to have a strong association with heart disease and heart disease. Long before there was heart disease, hypercortisolemia and consequent sympathetic hyperactivity caused by emotional stress showed how the body/mind relationship should be considered.

In this context, encouraging the biopsychosocial look at the patient, the concern arises to research more about Takotsubo cardiomyopathy (CMT), which is conceptually known as Takotsubo's disease, broken heart syndrome or stress-induced cardiomyopathy. CMT can be characterized as a transient and segmental disorder of the left ventricle (LV) in the absence of obstructive coronary artery disease, being caused, in most cases, by a situation of acute emotional or physical stress<sup>2</sup>. Its pathophysiology is not well defined, however, the literature shows some pathophysiological mechanisms, such as coronary spasms, microvascular dysfunction, transient coronary occlusion, estrogen deficiency and sympathetic changes, induced by increased release of cortisol and catecholamines<sup>3</sup>.

Epidemiological data suggest that CMT is an underdiagnosed clinical condition, as it represents a rate of 1.7% to 2.2% of cases that are investigated after receiving an initial diagnosis of acute coronary syndrome<sup>4</sup>. Female gender and advanced age have a prevalence in Takotsubo Cardiomyopathy and 90% of cases reported bibliographically are postmenopausal women<sup>5</sup>.

That said, and considering the proposed pathophysiological mechanism of the pathology, this study is based on the following guiding question, what are the variables found in the literature that culminate in the diagnosis of Takotsubo Cardiomyopathy? The hypothesis for this question is that stressors increase the records of heart attacks, hypertensive crises, people with anxiety and depression<sup>5</sup>. All of this leads to a final condition of extreme stress, which triggers the development of Takotsubo Cardiomyopathy in genetically predisposed individuals.

The justification for this study is given by the information that heart disease is the main cause of mortality and morbidity worldwide<sup>6</sup>. Knowing this, studies have been published showing that 50% of the reduction in deaths from heart disease is due to evidence-based medical therapies, with the other half due to a reduction in risk factors through prevention through health education. As it is a disease often misdiagnosed and confused with Acute Myocardial

Infarction (AMI), despite having a distinct pathophysiology, CMT becomes one of the main differential diagnoses of AMI.

Therefore, the objective of this research is to identify studies that address the factors that can trigger Takotsubo cardiomyopathy to understand its pathophysiological mechanisms and diagnosis.

## Methodology

The methodology used in this study is an integrative literature review, based on the six classic steps of the method. The integrative review is the broadest methodological approach regarding reviews, allowing the inclusion of experimental and non-experimental studies for a complete understanding of the phenomenon analyzed. It combines data from theoretical and empirical literature, incorporating a wide and wide range of purposes: definition of concepts, review of theories and evidence, and analysis of methodological problems of a particular topic. The large sample, together with the multiplicity of proposals, should generate a consistent and understandable panorama of complex concepts, theories, or health problems relevant to the health-disease context<sup>9,10</sup>.

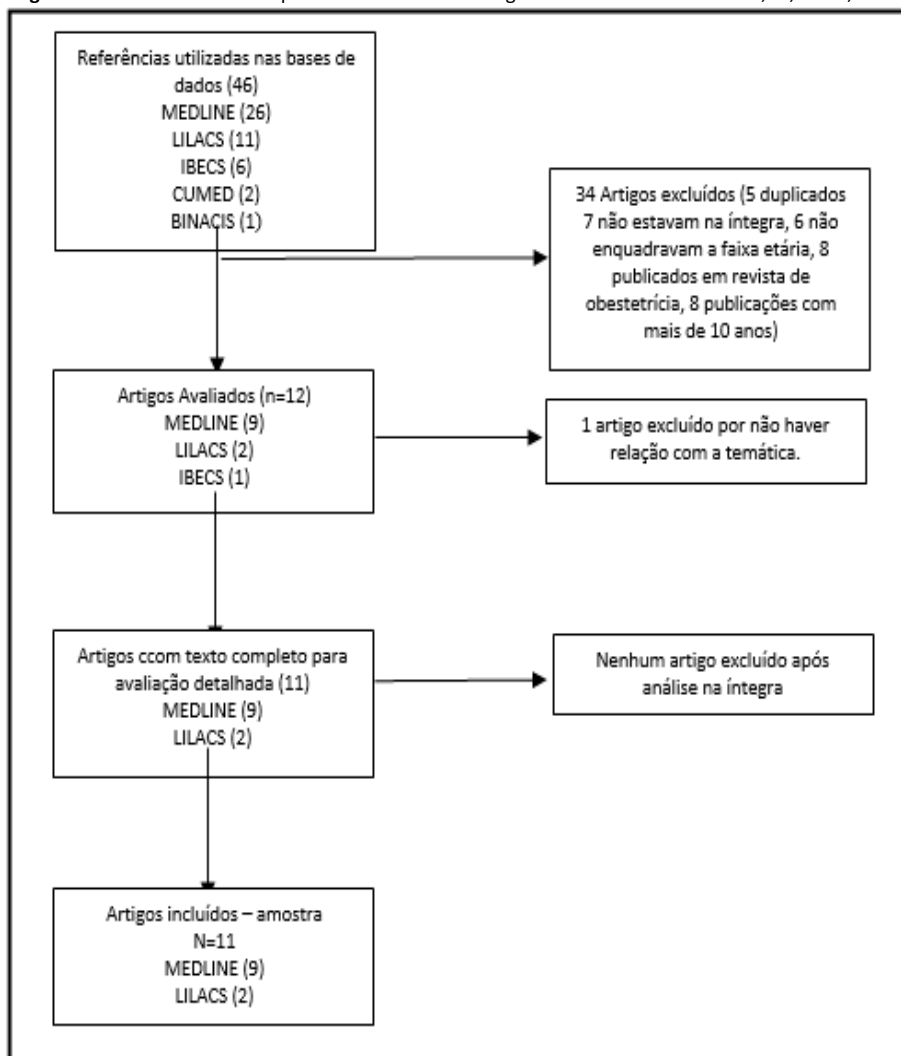
To answer the objective of the study, the acronym PVO was used as a method, where "P" indicates the research disease; "V" the variables and "O" the outcome, which are described below P – Takotsubo cardiomyopathy; V – Risk factors; O – Diagnosis.

Data were collected by searching for articles in the Virtual Health Library database platform, where we were able to retrieve material from LILACS, MEDLINE, IBECs, BINACIS and CUMED databases. In the strategy, the descriptors "Takotsubo Cardiomyopathy" "Risk Factors" "Diagnosis" were used using the following strategies and Boolean operator: "Takotsubo Cardiomyopathy AND Risk Factors AND Diagnosis"; "Takotsubo Cardiomyopathy AND Risk Factors"; "Takotsubo Cardiomyopathy AND Diagnosis".

The inclusion criteria used were articles published less than 10 years ago, studies in human beings over 18 years old, journals in the field of cardiology, medicine, diagnostic imaging, vascular diseases, and the exclusion criteria were expanded abstracts, review articles and recovered material that did not meet the methodology. A total of 12 articles were retrieved and, after peer review using the adapted URSI criteria, 11 studies remained for analysis (Figure 1).

For data extraction, a spreadsheet was made in Microsoft Word® software that included the authors, country, year of publication, study method, objectives, results, and outcome of the studies.

Figure 1. Flow of the selection process of articles for integrative review. Rio de Janeiro, RJ, Brazil, 2021



**Results**

Of the eleven articles analyzed, two were developed in the United States, two in Mexico, one in Germany, one in Japan, one in Turkey, one in South Korea,

one in Colombia, one in Portugal and one in Chile. Of these, eight were published in English and three in Spanish. The analyzed articles contemplated the theme proposed by the PVO strategy, which are described in Chart 1.

Chart 1. General characteristics of the included studies on Takotsubo Cardiomyopathy, diagnosis, and outcomes. Rio de Janeiro, RJ, Brazil, 2021

Title	Authors	Study method	Contributions
Takotsubo cardiomyopathy in a patient with previously undiagnosed hypertrophic cardiomyopathy with obstruction	Brabham WW, Lewis GF, Bonnema DD, Nielsen CD, Brien TX. 2011	Case report	Supported by other literature, they suggested that left ventricular outflow tract obstruction may favor the development of Takotsubo Cardiomyopathy.
Bail-Out Alcohol Septal Ablation for Hypertrophic Obstructive Cardiomyopathy in a Patient with Takotsubo Cardiomyopathy Induced Cardiogenic Shock	Sossalla S, Meindl C, Fischer M, Lubnow M, Müller T, Maier LS., 2019	Case report	Alcoholic septal ablation may be effective for the treatment of refractive cardiogenic shock diseases due to a combination of Takotsubo cardiomyopathy and hypertrophic obstructive cardiomyopathy.
Basal wall hypercontraction of Takotsubo cardiomyopathy in a patient who had been diagnosed with dilated cardiomyopathy: a case report	Ichihara N, Fujita S, Kanzaki Y, Fujisaka T, Ozeki M, Ishizaka N, 2017	Case report	The clinical profile presented by the case patient can provide important information about the possibility of chronic or recurrent Takotsubo cardiomyopathy as the underlying cause of dilated cardiomyopathy.
Concomitant hypertrophic and takotsubo cardiomyopathy; cardiac magnetic resonance	Yalcinkaya D, Yarlioglu M, Yigit H, Duran	Case report	The successful use of magnetic resonance imaging for the concomitant diagnosis of Takotsubo cardiomyopathy and hypertrophic cardiomyopathy.



with parametric mapping findings after acute phase	M, Murat SN et al, 2019		
Evolutionary Change Mimicking Apical Hypertrophic Cardiomyopathy in a Patient with Takotsubo Cardiomyopathy	Hwang HJ, Lee HM, Yang IH, Kim DH, Byun JK, Sohn IS, 2014	Case report	Transient myocardial thickening caused by myocardial edema involved in Takotsubo Cardiomyopathy, simulating apical hypertrophy. Thickening remained present even during recovery.
Miocardio patía de takotsubo y la arteria coronaria única: una combinación excepcional	Marín SS, Franklin H, Nestor R, Valencia JM, 2015	Case report	Takotsubo syndrome is a type of acquired, transient and reversible cardiomyopathy, which is diagnosed by differential means, by investigating and ruling out acute myocardial infarction with or without ST-segment elevation. When this syndrome presents with ST-segment elevation in precordial leads, it can be difficult to differentiate from an acute coronary event.
Miocardio patía de Takotsubo: cuando las coronarias callan	Cardona VJ, Ceballos NL, Torres SS, 2018	Case report	Importance of knowing the natural history and pathophysiological mechanism of heart disease to provide an adequate diagnosis.
Myocardial dysfunction in Takotsubo syndrome: More than meets the eye?	Pestana G, Tavares SM, Sousa C, Pinto R, Ribeiro V, Vasconcelos M, et al., 2017	Retrospective observational study	Less contraction force was observed in the inferolateral basal segments and greater mean longitudinal deformation in the LV basal segments in patients with Takotsubo Syndrome compared to patients with IAMCSST.
Recurrencia de miocardio patía por estrés posterior a terremoto en Chile. Reporte de un caso clínico	Varela CU, Bohn RR, Varleta PO, Concepción RC, 2011	Case report	Recurrence variability is due to the number of stressful events during life, which exceed the limit of adrenergic response, triggering a high discharge of catecholamines causing observed motility changes, producing morphological changes in cardiomyocytes and homeostasis disorders.
Stress Cardiomyopathy in a Patient with Hypertrophic Cardiomyopathy: Case Presentation and Review of the Literature	Vinardell JMM, Christos GN, Adam RO, Richard E, Esteban SO, 2018	Case report	Hypertrophic cardiomyopathy and Takotsubo cardiomyopathy can coexist, the latter having a worse prognosis in the acute phase when there is involvement of the mitral valve.
Stress induced cardiomyopathy due to a Mexican earthquake	Fernández FR, Morales VN, Herrera GM, Alcántara MMA, García GM, González CO, et al, 2018	Case report	There is no established worldwide consensus for the diagnosis of Takotsubo cardiomyopathy, and the Mayo Clinic criteria are widely used in clinical practice and in research.

## Discussion

Takotsubo cardiomyopathy (CMT) is underdiagnosed because its findings are confused with Acute Coronary Syndrome (ACS), which makes it difficult to distinguish between pathologies and, consequently, the treatment used. The evidence found through the retrieved articles indicates the association of CMT with stressors, both physical and psychological, being these the most likely variables. There are also signs of recurrence of disease recurrence in individuals previously diagnosed where the stressors were not stopped.

The diagnosis of CMT is conducted through the patient's clinical history and the performance of some complementary exams such as ECG, which may present findings that confuse with acute myocardial infarction such as ischemic area with or without ST segment elevation, left ventricular systolic dysfunction (VE) which culminates in a low ejection fraction, however CMT has a regional pattern of worse basal longitudinal deformation than AMI CS ST.

Still in relation to diagnosis, it is worth noting that there are no universally defined criteria to perform it, however, the most used criterion is the Mayo Clinic,

proposed in 2004 and adapted in 2008<sup>10,15</sup>. According to this criterion, the patient must have all the following characteristics<sup>10,11</sup>.

Hypokinesia, akinesia or transient dyskinesia of the middle segment of the left ventricle, with or without apical involvement. The change must extend beyond the irrigation territory of an epicardial artery. Absence of obstructive coronary disease. Absence of myocarditis, pheochromocytoma, hypertrophic cardiomyopathy<sup>16</sup> or myocardial dysfunction of different etiology. Electrocardiographic alteration demonstrating ST-segment elevation and T-wave inversion or mild troponin elevation. As shown, there is no consensus on the criteria to be used for the diagnosis of CMT, however, according to Mayo's criteria, CMT cannot coexist with hypertrophic cardiomyopathy, however, in the report presented by<sup>12</sup>, we see the case of a patient with both conditions. In addition, the same author also cites 14 other similar cases reported in the literature<sup>13</sup>.

In 90% of cases<sup>10</sup>, the patient's clinic will be precordial pain with or without sudden onset dyspnea, however, the presentation may vary from mildly



symptomatic patients to critically ill patients<sup>16</sup>. As seen in the case reports of 14 on the patient who presented with CMT after an earthquake in Mexico, there is usually an emotional or stress trigger associated with the onset of the syndrome, but it is not necessarily present, or sometimes not identified. A manifestation that rarely occurs in patients with CMT is cardiogenic shock<sup>10,16</sup>, however, when present, it configures a cardiac emergency, requiring immediate detection and treatment. The prognosis of the pathology is generally favorable, even in cases where CMT evolves into cardiogenic shock<sup>15</sup>.

## Conclusion

The results of the present study demonstrate the association of stressors with the development of Takotsubo Cardiomyopathy, clarifying possible relationships between them. It is necessary to give light and emphasis to this theme because the clinical manifestations of this syndrome are like those of other coronary pathologies such as AMI. Identifying such a condition is of fundamental importance to determine the therapeutic approach, which confirms the need to better understand the triggering agents of the disease, and the adoption of health actions for the prevention of CMT.

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