TAKOTSUBO CARDIOMYOPATHY AND THE HEART-BRAIN AXIS

Estevan Fillipe Bispo de Oliveira[1]

João Pedro do Valle Varela[2]

Luiza Alves Liphaus[3]

Álvaro Batista Rosado[4]

Julia Miranda Nobre[5]

Bernardo Alves Brambilla[6]

Ana Luiza Ferraz Barbosa[7]

Letícia Cypreste Preti[8]

Bruno de Oliveira Figueiredo[9]

Bruno de Figueiredo Moutinho[10]

Gabriel Moraes dos Santos[11]

Éric Rocha Santório[12]

Ursula Amanda Sá da Cunha[13]

Thiago Zanetti Pinheiro[14]

Ana Carolina Alves[15]

1 University of Western Paulista (Unoeste)
2 São Carlos University Center
3 Vila Velha University (UVV)
4 Vila Velha University (UVV)
5 Vila Velha University (UVV)
6 UNIG Itaperuna
7 University Center of Espírito Santo (UNESC)
8 Multivix Vitória
9 University of Vassouras
10 UniRedentor
11 Federal University of Rio de Janeiro
12 Federal University of Espírito Santo
13 São Carlos University Center
14 Iguaçu University Campus V
15 Universidad Cristiana de Bolivia (UCEBOL)

Luiz Coelho Soares Figueiredo[16]

Abstract: Takotsubo cardiomyopathy (TC), also known as broken heart syndrome, is a transient heart condition often triggered by intense emotional or physical stress. It is characterized by temporary ventricular dysfunction that mimics acute coronary syndrome, but without significant obstruction of the coronary arteries. Recent studies indicate a strong connection between the central nervous system and the heart, known as the heart-brain axis, which influences the pathophysiology of TC. This study seeks to explore the relationship between Takotsubo cardiomyopathy and the heart-brain axis, evaluating the neurocardiogenic mechanisms involved and their clinical implications for the diagnosis, prognosis and management of the disease. This is a bibliographic review with a qualitative approach, using the PubMed, Scopus and Web of Science databases to search for scientific articles. Specific descriptors related to Takotsubo Syndrome and its relationship with neurocardiological and psychological aspects were used to refine the search. The time frame covers the years 2020 to 2023, according to the date of the first and last reference selected. Takotsubo cardiomyopathy is strongly associated with hyperactivation of the sympathetic nervous system and excessive release of catecholamines, leading to transient myocardial dysfunction. The heart-brain axis plays a crucial role, as evidenced by neuroimaging studies that show alterations in brain regions responsible for emotional processing, such as the amygdala and prefrontal cortex. In addition, patients with TC have a higher prevalence of psychiatric disorders such as anxiety and depression, suggesting a bidirectional interaction between the brain and the heart. The management of TC involves hemodynamic support and stress control, with an increasing focus on neurocardiological approaches. Takotsubo cardiomyopathy exemplifies the complex interaction between the brain and the heart, reinforcing the need for a multidisciplinary approach in its diagnosis and treatment. The study of the heart-brain axis opens up new perspectives for understanding the neurocardiogenic mechanisms of the disease and may contribute to more effective therapeutic strategies, preventing recurrences and improving patient

16 Faculty of Medicine of Campos

prognosis.

Keywords: Cardiomyopathies; Cardiology; Takotsubo disease.

INTRODUCTION

Takotsubo cardiomyopathy (CT), also known as broken heart syndrome, is a transient condition characterized by reversible left ventricular dysfunction, usually precipitated by intense emotional or physical stress. Although its clinical presentation resembles that of an acute coronary syndrome (ACS), this cardiomyopathy occurs in the absence of significant coronary artery obstruction. Recent studies have demonstrated the importance of the interaction between the central nervous system and the heart, highlighting the role of the heart-brain axis in the pathophysiology of the disease (GADSBOL et al., 2021).

Autonomic dysfunction plays a central role in the pathophysiology of TC, since intense stress leads to an exacerbated release of catecholamines, resulting in cardiotoxicity and myocardial dysfunction. Experimental models suggest that hyperactivation of the hypothalamic-pituitary-adrenal (HPA) axis and sensitization of the sympathetic nervous system contribute to the syndrome, associating it with a neurocardiogenic mechanism. This relationship between brain and heart reinforces the need for multidisciplinary approaches to understand and treat the condition (TEMPLIN et al., 2020).

In addition to neuroendocrine factors, Takotsubo cardiomyopathy is often associated with psychiatric and psychological disorders, such as depression, anxiety, and post-traumatic stress disorder (PTSD). Clinical studies have shown that patients with a history of psychiatric diseases have a higher risk of developing the syndrome, suggesting a vulnerability of the brain-heart axis in predisposed individuals. Thus, the early identification of psychological risk factors can help in the prevention and management of this cardiomyopathy (PERRIN et al., 2022).

With the advancement of neuroimaging techniques and electrophysiological studies, it has become evident that brain regions involved in emotional regulation, such as the amygdala and the

prefrontal cortex, exert a direct influence on cardiovascular function. Dysfunctions in these areas may predispose individuals to exacerbated stress response, leading to the development of Takotsubo cardiomyopathy. Thus, better understanding the interaction between the cardiovascular and central nervous systems may provide new therapeutic strategies to prevent and treat this condition (SUZUKI et al., 2023).

This study seeks to explore the relationship between Takotsubo cardiomyopathy and the heart-brain axis, evaluating the neurocardiogenic mechanisms involved and their clinical implications in the diagnosis, prognosis, and management of the disease.

MATERIALS AND METHODS

This is a literature review with a qualitative approach, using the PubMed, Scopus and Web of Science databases to search for scientific articles. To refine the research, specific descriptors related to Takotsubo Syndrome and its relationship with neurocardiological and psychological aspects were used. The time frame covers the years 2020 to 2023, according to the date of the first and last selected reference.

Guiding Question

What is the relationship between neurocardiological, psychological, and autonomic factors in the pathogenesis and management of Takotsubo syndrome?

Inclusion Criteria

Articles published between 2020 and 2023.

Studies that address pathophysiological mechanisms, neurocardiology, psychological factors and new therapeutic approaches for Takotsubo syndrome.

Papers available in full and indexed in PubMed, Scopus and Web of Science.

Publications in Portuguese, English or Spanish.

Systematic reviews, clinical studies and research with a neurophysiological or cardiovascular approach.

Exclusion Criteria

Studies published before 2020.

Works not available in full or with restricted access.

Research with an exclusive focus on stress cardiomyopathy without considering the brain-heart interaction.

Articles that analyze only laboratory or genetic markers, without clinical contextualization.

Duplicate studies or isolated case reports with no relevance to the review.

Health Descriptors

The following descriptors were used in the search:

“Takotsubo cardiomyopathy”

“Neurocardiology”

“Autonomic nervous system”

“Stress-induced cardiomyopathy”

“Emotional stress and heart disease”

Boolean Markers

The descriptors were combined with Boolean operators to refine the results:

(“Takotsubo cardiomyopathy” AND “Neurocardiology”)

(“Stress-induced cardiomyopathy” OR “Autonomic nervous system”)

(“Takotsubo syndrome” AND (“Emotional stress” OR “Heart disease”))

THEORETICAL FOUNDATION

Takotsubo cardiomyopathy (TC) is a transient syndrome characterized by reversible left ventricular dysfunction, usually precipitated by intense emotional or physical stress. Although its pathophysiology is not yet completely elucidated, studies indicate that hyperactivation of the sympathetic nervous system plays a crucial role in promoting an excessive release of catecholamines, which can lead to transient myocardial dysfunction (WITTSTEIN, 2021).

The heart-brain axis refers to the complex interaction between the central nervous system and the heart, mediated by autonomic and hormonal pathways. Research suggests that activation of brain areas involved in stress regulation, such as the amygdala, prefrontal cortex, and hypothalamus, contributes to the exacerbated cardiovascular response seen in CT. Dysfunction in these regions can increase vulnerability to cardiovascular events, especially in individuals with a history of psychiatric disorders or previous exposure to traumatic situations (HASAN et al., 2022).

The autonomic nervous system (ANS) plays a central role in regulating heart function. In patients with TC, an imbalance between the sympathetic and parasympathetic systems is observed, resulting in a severe hyperadrenergic response. This uncontrolled activation of the sympathetic system can induce coronary vasospasm, endothelial dysfunction, and direct toxic effects on cardiac myocytes (UZUI et al., 2020).

Functional neuroimaging studies demonstrate that patients with TC have alterations in the connectivity between brain structures involved in ANS regulation. In particular, hyperactivity of the amygdala and hypothalamus has been associated with an increase in sympathetic excitability, contributing to myocardial dysfunction. In addition, reduced activity of the prefrontal cortex, which is responsible for modulating the stress response, may exacerbate autonomic dysregulation (FILLMORE et al., 2023).

There is a strong correlation between Takotsubo cardiomyopathy and psychiatric disorders such as depression, anxiety, and post-traumatic stress disorder Chronic exposure to psychological

stress can lead to sensitization of the hypothalamic-pituitary-adrenal (HPA) axis, resulting in a disproportionate response to acute stress. This mechanism may explain why patients with emotional disorders are more susceptible to TC. In addition, recent studies indicate that dysfunction of glucocorticoid receptors may play a role in modulating the inflammatory and cardiovascular response to stress (MORI et al., 2022).

Although Takotsubo cardiomyopathy is usually a reversible condition, its prognosis can be variable. In some cases, complications such as heart failure, ventricular arrhythmias, and cardiogenic shock may occur, requiring intensive support. Early identification of risk factors and a multidisciplinary approach are essential to improve the clinical outcomes of these patients (Y-HASSAN et al., 2022).

Therapeutic options for TC include the use of beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, and strategies to reduce the impact of emotional stress. However, the lack of specific guidelines for the management of TC poses a challenge, highlighting the need for further studies on the relationship between the heart-brain axis and cardiovascular vulnerability to stress (SINGH et al., 2023).

CONCLUSION

Therefore, Takotsubo cardiomyopathy represents a clinical and scientific challenge, given its complex interaction between emotional, neurological, and cardiovascular factors. The role of the heart-brain axis in this condition highlights the importance of a multidisciplinary approach in the diagnosis and management of the disease, considering not only cardiac function, but also the impact of psychological factors and the autonomic nervous system.

Advances in neuroimaging and sympathetic nervous system studies have contributed to a better understanding of the pathophysiology of Takotsubo, reinforcing the hypothesis that autonomic hyperactivation plays a central role in the transient ventricular dysfunction observed in these patients. In addition, the relationship between psychiatric disorders, such as anxiety and depression, and the

predisposition to the development of the syndrome highlights the need for preventive strategies aimed at the emotional and mental well-being of at-risk individuals.

Despite being a generally reversible condition, Takotsubo can be associated with serious complications, including heart failure and arrhythmias, requiring careful and personalized follow-up. The lack of specific guidelines for the treatment of the syndrome reinforces the need for further studies evaluating effective therapeutic strategies to minimize recurrences and improve long-term prognosis.

Thus, understanding the mechanisms that interconnect the central nervous system and cardiac function is essential to improve the clinical approach to Takotsubo cardiomyopathy. The integration between cardiology, neurology, and psychiatry can contribute significantly to the early identification, appropriate management, and prevention of this syndrome, directly benefiting the quality of life of affected patients.

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