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THERAPEUTIC APPROACH AND CLINICAL MANAGEMENT OF TAKOTSUBO CARDIOMYOPATHY: BROKEN HEART SYNDROME

ABORDAGEM TERAPÊUTICA E MANEJO CLÍNICO DA MIOCARDIOPATIA DE TAKOTSUBO: SÍNDROME DO CORAÇÃO PARTIDO

ENFOQUE TERAPÉUTICO Y MANEJO CLÍNICO DE LA MIOCARDIOPATÍA DE TAKOTSUBO: SÍNDROME DEL CORAZÓN ROTO

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ABSTRACT

Takotsubo Cardiomyopathy (TTC), also known as “Broken Heart Syndrome,” is a form of acute and transient heart failure, often triggered by intense emotional or physical stressors. This study aimed to review current scientific evidence on the clinical management and therapeutic strategies for this condition. It is a narrative literature review based on recent scientific articles discussing the pathophysiology mediated by a “catecholamine storm,” diagnostic criteria, and therapeutic escalation. The results indicate that, although TTC has historically been considered benign, it carries risks of mortality and acute complications comparable to Acute Coronary Syndrome (ACS). Management should be individualized, focusing on hemodynamic stabilization, respiratory support, and, in severe cases, the use of mechanical circulatory support, avoiding inotropic agents in patients with left ventricular outflow tract obstruction (LVOTO). It is concluded that prompt differential diagnosis and long-term follow-up with renin–angiotensin–aldosterone system inhibitors are essential to reduce morbidity and prevent recurrence.

Keywords: Takotsubo Cardiomyopathy. Therapeutics. Diagnosis. Heart Failure.

RESUMO

A Miocardiopatia de Takotsubo (TTC), ou "Síndrome do Coração Partido", é uma forma de insuficiência cardíaca aguda e transitória, desencadeada frequentemente por estressores emocionais ou físicos intensos. O presente estudo teve como objetivo revisar as evidências científicas atuais sobre o manejo clínico e as estratégias terapêuticas para essa condição. Trata-se de uma revisão narrativa da literatura, fundamentada em artigos científicos recentes que discutem a fisiopatologia mediada pela "tempestade de

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catecolaminas", os critérios diagnósticos e o escalonamento terapêutico. Os resultados indicam que, embora a TTC tenha sido historicamente considerada benigna, ela apresenta riscos de mortalidade e complicações agudas comparáveis à Síndrome Coronariana Aguda (SCA). O manejo deve ser individualizado, focando na estabilização hemodinâmica, suporte respiratório e, em casos graves, no uso de suporte circulatório mecânico, evitando-se inotrópicos em pacientes com obstrução do trato de saída do ventrículo esquerdo (OTSVE). Conclui-se que o diagnóstico diferencial ágil e o acompanhamento a longo prazo com inibidores do eixo renina-angiotensina-aldosterona são fundamentais para reduzir a morbidade e prevenir recorrências.

Palavras-chave: Cardiomiopatia de Takotsubo. Terapêutica. Diagnóstico. Insuficiência Cardíaca.

RESUMEN

La Miocardiopatía de Takotsubo (TTC), también conocida como “Síndrome del Corazón Roto”, es una forma de insuficiencia cardíaca aguda y transitoria, frecuentemente desencadenada por estresores emocionales o físicos intensos. El presente estudio tuvo como objetivo revisar la evidencia científica actual sobre el manejo clínico y las estrategias terapéuticas para esta condición. Se trata de una revisión narrativa de la literatura, basada en artículos científicos recientes que abordan la fisiopatología mediada por una “tormenta de catecolaminas”, los criterios diagnósticos y la escalada terapéutica. Los resultados indican que, aunque la TTC ha sido considerada históricamente benigna, presenta riesgos de mortalidad y complicaciones agudas comparables al Síndrome Coronario Agudo (SCA). El manejo debe ser individualizado, centrado en la estabilización hemodinámica, el soporte respiratorio y, en casos graves, el uso de soporte circulatorio mecánico, evitando el uso de inotrópicos en pacientes con obstrucción del tracto de salida del ventrículo izquierdo (OTSVI). Se concluye que el diagnóstico diferencial oportuno y el seguimiento a largo plazo con inhibidores del sistema renina-angiotensina-aldosterona son fundamentales para reducir la morbilidad y prevenir recurrencias.

Palabras clave: Miocardiopatía de Takotsubo. Terapéutica. Diagnóstico. Insuficiencia Cardíaca.

1 INTRODUCTION

Takotsubo Cardiomyopathy (TTC) is a syndrome of acute and transient left ventricular (LV) systolic dysfunction that does not follow the distribution pattern of an epicardial coronary artery (Assad et al., 2022; Matta et al., 2023). It is morphologically characterized by apical ballooning — resembling a Japanese octopus trap, from which it derives its name —, although variants such as basal ("reverse"), mesoventricular and focal are increasingly recognized (Matta et al., 2022; Dave et al., 2024). The condition predominantly affects postmenopausal women, accounting for about 2% of all patients presenting with suspected acute myocardial infarction (ACS) (Assad et al., 2022).

The pathogenesis of TTC is intrinsically linked to an exacerbated sympathetic response and a "catecholamine storm", which result in myocardial daze via direct toxicity, microvascular spasm, and endothelial dysfunction (Singh et al., 2022; Matta et al., 2023). The trigger can be emotional (grief, fear) or physical (surgery, sepsis, severe pain), and in rare cases, it can occur in the peripartum period (Pillitteri et al., 2024; Murphy et al., 2025). Although recovery of left ventricular ejection fraction (LVEF) usually occurs within days or weeks, the acute phase is critical due to the risk of cardiogenic shock, fatal arrhythmias, and left ventricular outflow tract obstruction (LVOTS) (Singh et al., 2022; Matta et al., 2022). In view of the diagnostic complexity and the potential for severity, the analysis of clinical management protocols is imperative.

2 METHODOLOGY

This study is a narrative literature review, elaborated with the objective of synthesizing recent scientific evidence on therapeutic approaches and clinical management of Takotsubo Cardiomyopathy. The search was conducted in the PubMed database, using the descriptors "Takotsubo cardiomyopathy", "Therapeutics" and "Diagnosis", combined by Boolean operators. Articles published between 2021 and 2026, written in English or Portuguese, covering systematic reviews, guidelines, and complex clinical case reports, were included. Studies with low methodological rigor or that did not directly address therapeutic management were excluded. The selection of studies was carried out by screening titles and abstracts, followed by the full analysis of the texts to confirm relevance and scientific reliability.

3 RESULTS

The contemporary scientific literature establishes that the differential diagnosis between TTC and ACS is the first and most crucial clinical challenge. The results demonstrate that coronary angiography remains essential to rule out obstructive coronary artery disease, which can coexist with TTC in up to 10-15% of cases (Assad et al., 2022). Cardiac Magnetic Resonance Imaging (CMR) has emerged as the gold standard for confirmatory diagnosis, allowing the visualization of myocardial edema and the absence of delayed gadolinium enhancement, which differentiates TTC from infarction and myocarditis (Matta et al., 2022; Singh et al., 2022).

Regarding **acute pharmacological management**, the guidelines suggest:

- **Stable Patients:** Standard treatment for heart failure with diuretics and vasodilators to reduce lung congestion (Singh et al., 2022).
- **Prevention of Thromboembolism:** In patients with LVEF $< 30\%$ and pronounced apical ballooning, prophylactic anticoagulation for at least 3 months is recommended to mitigate the risk of intraventricular thrombi (Assad et al., 2022; Singh et al., 2022).
- **Shock Management:** Identification of LVOTS via echocardiogram is vital. If LVOTS are present, inotropes (dobutamine, adrenaline) and the Intra-Aortic Balloon (IABP) are **contraindicated**, as they increase the pressure gradient and aggravate shock. In these cases, the use of beta-blockers and cautious volume replacement are preferred (Matta et al., 2022; Singh et al., 2022).

For **long-term management**, angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) have shown a benefit in survival and reduced recurrences, while the evidence for chronic use of beta-blockers alone remains inconclusive (Assad et al., 2022; Matta et al., 2023). Specific reports highlight the importance of multidisciplinary support in perioperative and peripartum settings, where invasive monitoring and mechanical circulatory support (such as VA-ECMO) may be required as a bridge to myocardial recovery (Pillitteri et al., 2024; Murphy et al., 2025).

4 DISCUSSION

Scholarly discussion of TTC refutes the historical perception that the syndrome is a "benign" condition. Singh et al. (2022) point out that the long-term burden of morbidity is significant, with many patients persisting with symptoms of fatigue and microvascular

dysfunction even after LVEF normalizes. The "inotrope paradox" is a central point of debate: in TTC, the same beta-adrenergic receptors that are supposed to help with contractility can switch signaling to an inhibitory pathway, making inotropes not only ineffective, but potentially toxic to the myocardium (Matta et al., 2023).

The "reverse" variant (basal ballooning), although rare, requires extra attention in young patients and in critical states of acute physiological stress (Dave et al., 2024). One challenge discussed is the therapeutic gap to prevent direct toxicity from catecholamines. While ACE inhibitors/ARBs focus on secondary remodeling and prevention, new strategies targeting the brain-heart axis and patients' mental health are essential, given that previous psychiatric disorders increase vulnerability to the syndrome (Assad et al., 2022; Singh et al., 2022). Finally, successful perioperative management depends on early identification of the surgical trigger and prompt hemodynamic stabilization to avoid multiorgan failure (Pillitteri et al., 2024).

5 CONCLUSION

Takotsubo Cardiomyopathy (TTC) should no longer be recognized as a benign condition, but rather as an acute syndrome with mortality risks and complications comparable to Acute Coronary Syndrome (ACS). Immediate clinical management requires an agile differential diagnosis, excluding obstructive coronary disease, and an individualized therapeutic approach.

Image-guided hemodynamic stabilization is crucial to identify Left Ventricular Outflow Tract Obstruction (LVOT), which dictates the contraindication of inotropes, due to their toxic potential and the "inotrope paradox", which can aggravate shock. Prevention of acute complications, such as thromboembolism and arrhythmias, and mechanical circulatory support (in refractory cases) complement the management of the critical phase.

In the long term, therapy with angiotensin-converting enzyme inhibitors (ACE) or angiotensin receptor blockers (ARBs) is the essential treatment for myocardial protection and the reduction of recurrences. Finally, given the significant long-term residual morbidity (fatigue and microvascular dysfunction) and the intrinsic link with stressors, follow-up must necessarily be continuous and multidisciplinary, integrating cardiology and psychological support to mitigate vulnerability and improve the overall prognosis of patients.

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