



EDITORIAL COMMENT

What is the role of estrogen in predisposition to Takotsubo syndrome throughout a woman's reproductive life?

Qual o papel dos estrogénios na predisposição à síndrome de Takotsubo ao longo da vida reprodutiva feminina?

Ana Rita Almeida

Hospital Garcia de Orta, Almada, Portugal

Available online 13 September 2022



Brás DR. et al. describe the case of a young woman who presents with a clinical picture compatible with Takotsubo syndrome five months after delivery.¹ This case is of particular interest because it is rare and highlights the likely influence of sex hormones, especially estrogen levels, on the occurrence of this cardiomyopathy. As this mechanism is still under investigation, it makes the case even more relevant.

As the authors point out, despite the higher incidence of Takotsubo syndrome in postmenopausal women, cases have been reported in premenopausal women, especially in the immediate postpartum period,^{2,3} but not only,⁴ thus suggesting that this cardiomyopathy occurs not only at menopause, but at other stages of reproductive life when estrogen levels are reduced.

The role of sex hormones in the development of Takotsubo cardiomyopathy has been a subject of interest and research, and it has been suggested that reduced levels of estrogen in menopause predispose women to Takotsubo syndrome.⁵ The young woman reported in this clinical case

was taking progesterone contraceptive pill and was breastfeeding, consequently presenting low levels of estrogen, which may have predisposed her to the development of this syndrome in the presence of a trigger (discussion/epileptic seizure).

Estrogen receptors are widely expressed in the cardiovascular system and in the central nervous system. Clinical analysis of autonomic nervous system function in patients with Takotsubo cardiomyopathy revealed a transient increase in sympathetic nervous system activity and a decrease in vagal activity.

Research has been carried out in rats,⁶ in which estrogen supplementation diminished the effects of catecholamines on the heart and attenuated stress-induced hypothalamic-sympathoadrenal discharge. It was found that in these rats estrogen supplementation increases the levels of cardioprotective substances such as atrial natriuretic peptide and the heat shock protein (HSP)704. This work suggests that the reduction of estrogen levels may lead to a predisposition to the development of this cardiomyopathy, either by direct action on the heart and indirect action on the nervous system.

E-mail address: anaalmeida31@gmail.com

<https://doi.org/10.1016/j.repc.2022.07.005>

0870-2551/© 2022 Sociedade Portuguesa de Cardiologia. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

However, conflicting results are observed in humans. In humans, there are no studies demonstrating that hormone replacement therapy in postmenopausal women prevents the occurrence of Takotsubo syndrome, and a Swiss registry showed that during Takotsubo syndrome in postmenopausal women estrogen levels are elevated.⁶

These results reinforce the need for more research in this area with randomized studies that allow us to better understand the influence of sex hormones, specifically estrogen, on the predisposition of women to Takotsubo syndrome throughout their reproductive life. The case presented by the authors has drawn attention to this problem, fueling interest in research in this area.

Conflicts of interest

The author has no conflicts of interest to declare

References

1. Brás DR, Semedo P, Piçarra BC, et al. Takotsubo Syndrome in a breast-feeding young woman: highlighting the protection of oestrogens? *Rev Port Cardiol.* 2022;41:887.
2. Citro R, Lyon A, Arbustini E, et al. Takotsubo Syndrome After Cesarean Section: Rare But Possible. *J Am Coll Cardiol.* 2018 Apr 24;71:1838–9.
3. Pires CM, et al. A life-threatening reverse TTS. *European Heart Journal - Case Reports.* 2021;5:1–8.
4. Kuo BT, Choubey R, Novaro GM. Reduced estrogen in menopause may predispose women to takotsubo cardiomyopathy. *Gend Med.* 2010;7:71–7.
5. Ueyama T, Kasamatsu K, Hano T, et al. Stress Neurotransmitters, and Hormones: *Ann. N.Y. Acad. Sci.* 2008;1148:479–85.
6. Brenner R, Weilenmann D, Maeder MT, Jorg L, Bluzaitė I, Rickli H, De Pasquale G, Ammann P. Clinical characteristics, sex hormones, and long-term follow-up in Swiss postmenopausal women presenting with Takotsubo cardiomyopathy. *Clin Cardiol.* 2012;35:340–7.