



## EDITORIAL COMMENT

## A double-edged sword at the intersection between cancer and cardiovascular disease

### A «faca de dois gumes» da combinação entre cancro e doença cardiovascular

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Cancer and cardiovascular diseases are the most common causes of death worldwide. In 2019, they were responsible for approximately half of the 58 million deaths in the world.<sup>1</sup>

Checkpoint-inhibitor immunotherapies are being increasingly used to improve the prognosis of several diseases. Briefly, these drugs modulate checkpoints that control our immune response, therefore increasing the ability of our immune system to kill cancer cells. It seems logical that drugs with this mechanism of action would be associated with nonspecific activation of the immune system, leading to the so-called off-target immune-related adverse events (detectable in 70–90% of patients). Myocarditis occurs in approximately 1% of patients on immune checkpoint inhibitors (ICI) and should be a leading differential diagnosis in “de novo” cardiovascular symptoms.<sup>2</sup>

The clinical case presented by Duarte et al.<sup>3</sup> highlights several challenges related to ICI-associated myocarditis: (1) most patients who develop myocarditis on ICIs have normal left ventricular ejection fraction before treatment is started; (2) there is no standard screening and surveillance strategy, but baseline echocardiogram and troponin measurement is recommended, thus providing a reference for future comparison if cardiovascular symptoms arise; (3) evidence-based guidance for the treatment of this complication is lacking, but several consensus documents

recommend early initiation of immunosuppression (corticosteroids as a first-line).

Interestingly, the diagnosis was confirmed by endomyocardial biopsy, still the old-school “gold standard” for the diagnosis of myocarditis. The debate surrounding its use and importance is out of the scope of this editorial. The critical highlight is that cardiac magnetic resonance (CMR) performed with standard tissue characterization and parametric mapping should be viewed as the “non-invasive biopsy” of the heart. CMR with myocardial mapping techniques is a helpful imaging test for the detection of myocardial inflammation in patients with suspected myocarditis, with a robust diagnostic accuracy that can circumvent the need for an endomyocardial biopsy.<sup>4</sup> The importance of the increasing availability of CMR in Portuguese cardiology departments cannot be overstated.

Cardio-oncology is an exciting and dynamic topic in cardiovascular medicine. A milestone was reached in 2022 with the publication of the first European guidelines specifically dedicated to this topic. The clinical case by Duarte et al.<sup>3</sup> illustrates one disease (myocarditis) associated with one type of cancer treatment (checkpoint immunotherapy) that is still largely unknown. Clearly, registries and clinical trials will be paramount to consolidating the growing body of evidence in the field of cardiovascular immune-related adverse

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events associated with ICI. In a broader perspective, the understanding of the complex interaction between cancer (and its therapies) and cardiovascular disease is pivotal for addressing the two most common causes of death in the world.

### Conflicts of interest

The author has no conflicts of interest to declare.

### References

1. Our World in Data (number of deaths by cause, World, 2019). Available from: <https://ourworldindata.org/grapher/annual-number-of-deaths-by-cause> [accessed 20.08.22].
2. Zhang L, Reynolds KL, Lyon AR, et al. The evolving immunotherapy landscape and the epidemiology, diagnosis, and management of cardiotoxicity: JACC: CardioOncology Primer. *JACC CardioOncol.* 2021;3:35–47.
3. Duarte T, Costa C, Gonçalves S, et al. A case of lymphocytic myocarditis in a patient treated with an immune checkpoint inhibitor, a recent class of chemotherapy agents. *Rev Port Cardiol.* 2022;41:1047–51.
4. Ferreira VM, Schulz-Menger J, Holmvang G, et al. Cardiovascular magnetic resonance in nonischemic myocardial inflammation: expert recommendations. *J Am Coll Cardiol.* 2018;72:3158–76.