Cardio-Oncology: Far Beyond Doxorubicin and the Tip of the Iceberg!

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Cardio-oncology is a new field of work and research on the adverse cardiovascular effects of cancer treatment, comorbidities and clinical conditions in cancer patients, and cardiovascular tumors. It has a wide spectrum ranging from arterial hypertension, arrhythmias, coronary and thromboembolic diseases to ventricular dysfunction, among others. In this special issue of ABC Heart Failure, we will focus on myocardial lesions, and consequently cardiomyopathies, ventricular dysfunction and heart failure (HF).

The Department of HF of the Brazilian Society of Cardiology has embraced Cardio-oncology since its beginning, by opening space for scientific discussion in its events and thematic area for abstract submissions, and now by offering this special issue addressing the main manifestations of endomyocardial/pericardial diseases and HF in cancer patients.

In these patients, cardiotoxicity used to be confused with left ventricular dysfunction and HF. Right after its discovery at the end of the 60s, higher and cumulative doses of anthracyclines were found to be associated with HF,[1,2] which was suggested by case reports. However, cardiotoxicity has remained unreported for a long time. The first works of oncology were not aimed at investigating cardiovascular adverse events, which were usually only reported when they became relevant clinical problems. HF is the severe, symptomatic, end-stage manifestation of myocardial injury. Thus, we only knew the visible tip of the iceberg.

With the speed required for the approval of new drugs in oncology, the methodological rigor has been neglected. The search for the cure of cancer has been considered more important to the detriment of potential adverse effects. Regulatory agencies have adopted a simplified system to approve new therapies in oncology. All contributed to keep clinical and subclinical manifestations of cardiotoxicity unnoticed by most people.

Scientific knowledge has increased *pari passu* with increasing publication of reports, from case reports, series, registries, pharmacovigilance studies to prospective, controlled, longitudinal studies. Anthracycline-induced ventricular dysfunction is current textbook knowledge; however, several other myocardial stressors have emerged. The old radiotherapy was revealed to be cardiotoxic, with late-onset lesions that are frequently associated with coronary, valve, pericardial and conduction system lesions. Other antineoplastic agents have joined the group of myocardial stressors, including cyclophosphamide-induced myocarditis, and ventricular dysfunction caused by the so-called "groundbreaking" target therapy, with the anti-HER2 monoclonal antibody, that revolutionized breast cancer treatment – the trastuzumab. Tyrosine kinase inhibitors, known as "oral chemotherapy", have been associated with hypertension, ventricular dysfunction, and HF with preserved ejection fraction. Immunotherapy, the fourth pilar of cancer treatment, has changed the paradigm as a new targeted treatment that strengthens patient's immune system, but with the side effect of an uncommon, difficult to be recognized, highly lethal myocarditis. Therefore, in cardio-oncology, many are the stressors to the myocardium and the villains.

We must face the multiple and eclectic challenges! Latin America is an example of a region with difficult access to the diagnosis and treatment of cancer.[3] We are far from achieving risk stratification of all patients diagnosed with cancer, which has been recently recommended by the European Society of Cardiology Guidelines on cardio-oncology.[4]

To know and early identify the mechanisms of myocardial lesion; stratify the risks; prevent; properly treat; rehab. The increase in the incidence of cancer and survival of the patients potentializes the increase in the prevalence.[5] There will be many patients and few qualified specialists. In parallel, we must share this new knowledge, in a didactic and strategic way under the epidemiological and clinical perspective. Brazil was the pioneer in publishing consensuses in the field,[6,7] and we need to rapidly democratize cardio-oncology, by means of articles, journals, events and courses.

Based on the exposed, cardio-oncology encompasses from the classical late-onset lesion caused by anthracycline in breast cancer patients to the acute myocarditis caused by immune checkpoint inhibitors and CART-T Tcells.[8] In this special issue of the ABC Heart Failure, we will address several clinical situations and clinical manifestations in the patient with cancer. For this purpose, we counted on the collaboration of some "explorers" in cardio-oncology in Brazil, enthusiasts and scholars who wrote the 19 articles of the issue. We thank the coauthors who kindly shared their time and knowledge. For readers, we hope this issue will be useful to help them navigating safely and finding out the exact dimension of the iceberg in front of us.

Keywords

Cardio-oncology; Chemotherapy/adverse effects; Oncology; Cardiology.

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