The epidemiologic transition witnessed in recent years enables us to predict that, in a few years, cancer will become the leading cause of death in the population in Western countries (Figure 1). Recent epidemiological data from the United States (US)\(^1\) has shown that neoplasms have already surpassed cardiovascular diseases as leaders in mortality in at least 22 North American states in 2012, compared with only two states in which cancer was the leading cause of death in 2000.

Oncology has achieved remarkable advances within the past decades, with the emergence of new treatments that are more effective and less toxic. However, a considerable number of complications is still observed with a remarkable number of cardiovascular complications. In an editorial published in this journal in 2012, Martins also alerted to the high rate of risk factors common to both cardiovascular diseases and cancer, such as smoking, overweight and obesity, sedentary lifestyle, diabetes mellitus, dietary pattern high in lipids and carbohydrates and low in fiber, dyslipidemias, alcoholism, and pollution.\(^2\)

The cardiovascular implications of the increased prevalence of neoplasms and the number of survivors of cancer are significant, since an increasing number of patients may present premature cardiovascular morbidity and mortality due to direct effects of cancer treatment in the structure and functioning of the cardiovascular system, as well as a worsening of pre-existing cardiovascular disease, especially in the presence of traditional cardiovascular risk factors.\(^3\)

The development of multidisciplinary teams to manage patients with oncologic diseases and risk of involvement of the cardiovascular system (or who already present cardiovascular complications) is a real necessity, and the specialty societies have been active in publishing recommendations to guide the approach to these patients,\(^2,7\) with the Brazilian Society of Cardiology being one of the pioneers in presenting its guideline in the year 2011.\(^4\) Cardio-oncology is a new subspecialty that has emerged in the area of intersection between cardiology and oncology from a need to improve care, define priorities, and deepen studies in the epidemiologic field elucidating the pathophysiology of the damage from cancer therapy to the cardiovascular system, allowing the development of effective strategies for prevention and treatment.

Anthracycline derivatives were the first to demonstrate to the scientific community the cardiotoxic potential of cancer treatment. With an efficacy beyond dispute in the treatment of various types of solid and hematological tumors, anthracyclines have a potential to inflict irreversible damage to the heart, which is associated with a significant mortality. Doxorubicin has an incidence of overall cardiotoxicity of 9%, and the rate of cardiac damage may reach up to 48% when doses of 700 mg/m\(^2\) are reached.\(^8\) Radiation therapy is also associated with adverse effects on the heart, such as pericarditis, valvular actinic lesions, and conduction disorders. However, even the exposure of the heart to doses considered low, as in patients with breast cancer, is associated with a 7.4% increase in the prevalence of coronary disease for each additional Gray of radiation dose to which the patient is exposed, especially in the presence of cardiovascular risk factors.\(^9\)

In the context of a well-defined dose-effect relationship, the limitation of accumulated doses, and the monitoring of the cardiac effect of the treatment are essential.\(^4\) A better understanding of these cardiotoxic associations has allowed clearer and more precise recommendations, like the ones recently published by the American Society of Clinical Oncology, which highlight the group of patients with an increased risk of cardiac dysfunction after cancer treatment (Table 1).

**Keywords**

Cardiovascular Diseases / epidemiology, Neoplasms / epidemiology, Oncology / trends.
Cancer treatments associated with an increased risk of cardiac dysfunction

1. High-dose anthracyclines (e.g., doxorubicin ≥ 250 mg/m², epirubicin ≥ 600 mg/m²).
2. High-dose radiotherapy (≥ 30 Gray) in which the heart is involved in the field.
3. Low-dose anthracyclines (e.g., doxorubicin < 250 mg/m², epirubicin < 600 mg/m²) in combination with low-dose radiotherapy (< 30 Gray), in which the heart is involved in the field.
4. Low-dose anthracyclines (e.g., doxorubicin < 250 mg/m², epirubicin < 600 mg/m²) or trastuzumab alone, in a patient with one of the following risk factors:
   - multiple cardiovascular risk factors during or after treatment (at least two): smoking, hypertension, dyslipidemia, obesity, and diabetes.
5. Low-dose anthracyclines (e.g., doxorubicin < 250 mg/m², epirubicin < 600 mg/m²) followed by treatment with trastuzumab (sequential therapy).

Source: Adapted from Armenian et al.7

With a well-defined group of patients at risk, physicians involved in these patients' care may implement strategies and protocols to monitor the effect of the treatment on the cardiovascular system.9 Imaging methods such as echocardiography, nuclear medicine, and magnetic resonance imaging have been decisively employed for very early detection of abnormalities in cardiac function and structure, preventing the development of changes interfering with the cardiovascular prognosis. We should also highlight the increasing use of biomarkers for this function, especially cardiac troponins.4

The new modalities for cancer treatment, such as target therapies, are also associated with cardiotoxicity; notably, the effect of trastuzumab, a monoclonal antibody against the epidermal growth factor receptor type 2 (HER2). Studies have shown that the incidence of symptomatic
heart failure in patients treated with trastuzumab is up to 5%, and the overall incidence of cardiac dysfunction may reach 19% of the patients, especially in the presence of cardiovascular risk factors and other potentially cardiotoxic treatments.10

In this context of the awakening of cardio-oncology, the IJCS draws attention from its readers for the coexistence between cancer and cardiovascular disease, which exceeds the limits of the direct toxic effect of cancer treatment and the sharing of cardiovascular risk factors. There are intricate associations between cancer and the heart, which can be itself the site of a neoplasm or be directly affected by tumor cells or by harmful substances produced by tumor cells, as is the case of cardiac carcinoid syndrome.3 A new scenario with the use of drugs such as angiotensin converting enzyme inhibitors and beta-blockers in cardiotoxicity prevention and reversal of damage is shaping up quickly due to these studies.8 Facing this entire scenario, we call on the scientific community interested in cardio-oncology to submit their works to the IJCS, which will be available to spread the information in this area of knowledge that will grow even more in importance in the coming years.

References


