## **SHORT EDITORIAL**

## Breast Cancer, Cardiotoxicity and Cardiovascular Disease Prevention: Where Are We in this Knowledge?

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Short Editorial referring to the article: Cardiovascular Disease in Women With Breast Cancer: A Contemporary Review

In recent decades, significant advances have been made in the early detection and treatment of different types of cancer, which have led to a significant worldwide increase in the number of survivors of this group of diseases, with estimates that two-thirds of all survivors would be 65 years old or older in 2020.

There are currently more than 32 million cancer survivors worldwide and this number is expected to continue growing, due to efficient screening for the disease and increased patient life expectancy after definitive treatment,<sup>3</sup> as well as increased life expectancy of populations, which increases the incidence of numerous neoplasms and is currently around 73.4 years worldwide for both sexes (70.8 years for men and 76 years for women).<sup>4</sup>

Despite evidence of a 34.9% reduction in cardiovascular mortality from 1990 to 2022,<sup>5</sup> cardiovascular diseases (CVD), represented by ischemic heart disease (the most common among CVDs), cerebrovascular diseases, rheumatic heart disease, heart failure (HF) and other conditions, remain the leading cause of death worldwide (17.9 million lives each year), and a third of these deaths occur prematurely in people under 70 years of age.<sup>6</sup>

Cancer is the second leading cause of death in the world, accounting for around 9.6 million deaths annually. In men, lung cancer (in addition to tracheal and bronchial cancers), prostate, colorectal, stomach, and liver cancers are the most common, while, in women, breast cancer (the main cause of cancer death in women), colorectal, lung,

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cervical, and thyroid cancers predominate.<sup>7</sup> Population aging and growth have led to a 33% increase in cancer cases, from 5.8 million in 2007 to 7.7 million in 2017, with most of this increase (20%) attributed to aging and 13% to population growth.<sup>1</sup>

Cardiac toxicity associated with chemotherapy for the treatment of cancer with anthracycline was initially described in 1967,8 the consequence of which leads to systolic ventricular dysfunction and HF.9 The evolution of knowledge in this area has demonstrated that cancer treatment, in its various modalities (chemotherapy, immunotherapy, radiotherapy), can compromise the cardiovascular system during the treatment or follow-up of survivors, leading to other CVDs and not just HF.9-11

In this context, cardiotoxicity is also related to the occurrence of acute and chronic coronary syndromes, atrial fibrillation, bradyarrhythmias, QT prolongation and ventricular arrhythmias, arterial hypertension, thrombosis and thromboembolic events (venous, arterial, and intracardiac), peripheral arterial disease, pulmonary hypertension, and pericardial diseases.<sup>9-11</sup>

Population aging, survival from breast cancer treatments, and the cardiovascular damage that these treatments can cause result in a large number of women (from the general population and from the group that survived breast cancer) at high cardiovascular risk.<sup>9-11</sup> As a consequence, CVD is currently the leading cause of death in women, regardless of whether they are breast cancer survivors or have never had this diagnosis.<sup>1</sup>

The article by Barragán et al., published here, presents a comprehensive review of numerous aspects of the association between breast cancer and CVD.<sup>12</sup>

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The authors draw attention to the existence of risk factors common to breast cancer (a neoplasm with the highest incidence and mortality in women) and CVD, the possible consequences for the cardiovascular system of the treatments currently used for that neoplasm (as well as the pathophysiological mechanisms involved), the strategies currently available for cardiovascular protection during chemotherapy and radiotherapy treatments, as well as the importance of CVD prevention (at all levels) at the time of neoplasm diagnosis and in those who survive treatment.<sup>12</sup>

The occurrence of common risk factors for both diseases (both with high morbidity and mortality in women) establishes the importance of investigating these and other cardiovascular risk factors, as well as the occurrence of CVD in any of its expressions, in patients who receive the diagnosis of breast cancer, considering that the appropriate management of these risk factors and diseases can minimize the risk of cardiotoxicity of the chosen treatments.<sup>9,11,13-15</sup>

Given their impact on the genesis of both diseases, shared risk factors (aging, western diet, physical inactivity, smoking, obesity, early menarche, hormonal therapy in menopause) should be targets of permanent health education policies for the population (including other cardiovascular or cancer risk factors), so that patients themselves, as well as health professionals, participate as actively as possible in primary prevention strategies for those diseases that can be prevented. <sup>13-15</sup> This knowledge becomes even more important for patients diagnosed with breast cancer for the protective adoption of secondary prevention strategies. <sup>9-11</sup>

Furthermore, knowledge about the existence of ventricular dysfunction, ischemic heart disease, arrhythmias, or other cardiovascular changes prior to the chemotherapy and/or radiotherapy treatment start will allow the optimization of the treatment of these conditions and greater care in monitoring patients undergoing treatment, for the recognition and appropriate management of decompensation or acute events.<sup>9-11</sup>

Barragán et al. clarify that the risk scores currently used to stratify cardiovascular risk in women with or even those without breast cancer do not include sex-specific cardiovascular risk factors, such as early menarche and hormonal treatment for menopause, which would be important in the cardiovascular risk stratification of women with breast cancer.<sup>12</sup> For this

reason, those authors reinforce the need to investigate and treat cardiovascular risk factors (independent, emerging, and exclusive to females)<sup>13-14</sup> and CVD prior to starting the cancer treatment, as well as during follow-up of survivors.<sup>12</sup>

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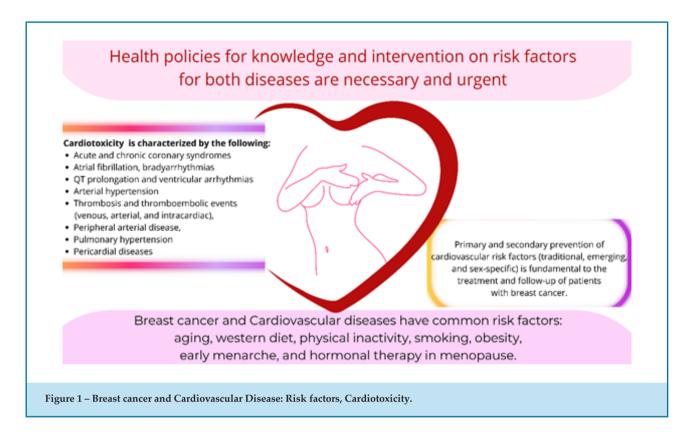
In addition, the authors mention the importance of researching the factors that contribute to the cardiotoxicity of chemotherapy and/or radiotherapy treatment to be carried out at the beginning and throughout the treatment, as well as in the follow-up of survivors.<sup>12</sup> The presence of these factors serves to classify patients who will undergo breast cancer treatment into low-, medium, and high-risk groups, with guidelines for the management of each group.<sup>12</sup> This set of long-term actions emphasizes the need to create working groups involving cardiologists and oncologists, as has been mentioned in numerous documents on this topic.<sup>9-11,15</sup>

From the point of view of cardioprotection for patients with breast cancer undergoing chemotherapy and/or radiotherapy treatment, the authors draw attention to the use of the lowest possible doses of chemotherapy drugs (Class I), 11 neurohormonal therapies (beta-blockers, renin-angiotensin-aldosterone system, angiotensin-converting enzyme inhibitors, mineralocorticoid receptor antagonists) and statins for the prevention of ventricular dysfunction (Class II), 11 iron chelators to prevent anthracycline toxicity (Class II), 11 and the reduction of heart exposure to radiation. 12 Moreover, they draw attention to the importance of primary and secondary prevention of cardiovascular risk factors for greater effectiveness of cancer treatment. 12

As in the article presented by Barragán et al., the various guidelines on Cardio-oncology also emphasize the importance of using current recommendations for the primary and secondary prevention of CVD in patients diagnosed with breast cancer and in those who survived treatment, considering the negative impact on cardiovascular morbidity during and after treatment, as well as the high cardiovascular mortality currently observed among survivors.<sup>9,11,15</sup>

Therefore, it is necessary to stratify the risk of cardiovascular toxicity in all patients diagnosed with breast cancer, and joint follow-up with the cardiologist should occur in those who have a previous diagnosis of CVD or who are at high risk for cardiotoxicity with the treatment to be initiated.<sup>11</sup>

Figure 1 presents the central idea of this editorial.



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