Middle Eastern Cancer and Oncology Journal (MECOJ)
ISSN: 3080-1427 (online) / 3080-1419 (print)
Volume 1, Issue 2 (April 2025 – June 2025), pp: 19-22

Commentary Article

Cardio-Oncology: Bridging the Gap Between Cardiovascular Health and Cancer Care

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Received: 12 March 2025 | Revised: 06April March 2025 | Accepted: 17 May 2025 | Published: 28 May 2025

Abstract

Cardio-oncology, an emerging subspecialty, is the study of the intersection of cardiovascular disease (CVD) and cancer. This field focuses on the prevention, diagnosis, and management of cardiovascular complications arising from cancer therapies. Given the increasing prevalence of cardiotoxicity induced by chemotherapy, targeted therapy, immunotherapy, and radiotherapy, this field plays a critical role in improving patient outcomes. Cardiotoxicity is characterized by a range of physiological manifestations, including cardiac dysfunction or heart failure, hypertension, arrhythmias, venous and arterial thromboembolism, pericardial disease, and pulmonary hypertension. Furthermore, the administration of certain pharmaceutical agents has been demonstrated to induce metabolic disturbances, which can manifest as an increased propensity for the development of diabetes or dyslipidemia, or the exacerbation of preexisting conditions. Chemotherapy-related cardiac dysfunction (CTRCD) manifests in two primary forms: type I, characterized by irreversible myocardial cell damage (e.g., anthracycline-induced cardiotoxicity), and type II, involving reversible myocardial dysfunction (e.g., trastuzumab-induced cardiotoxicity). Biomarkers, such as cardiac troponin (cTn) and natriuretic peptides (NP), play a pivotal role in the early detection of heart failure. Advanced imaging techniques, including cardiac MRI and speckle-tracking echocardiography, have been shown to enhance monitoring capabilities. Radiotherapy has been shown to have deleterious effects on cardiovascular health, contributing to the development of conditions such as coronary artery disease, valvular dysfunction, pericardial disease, and myocardial fibrosis. This review underscores the importance of multidisciplinary collaboration, early screening, and monitoring through innovative diagnostic tools to mitigate cardiovascular risks in cancer patients, ultimately enhancing survivorship and quality of life.

Keywords: *Cardio-oncology, Cardiotoxicity, Chemotherapy-Cardiotoxicity, Radiotherapy-Cardiotoxicity, Biomarkers.*

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Cite This Article: Skouri, H. N. (2025). Cardio-Oncology: Bridging the Gap Between Cardiovascular Health and Cancer Care. *Middle Eastern Cancer and Oncology Journal*, *1*(2), 19–22.
https://doi.org/10.61706/MECOJ160134

Introduction

The field of cardio-oncology, also known as onco-cardiology, emerged in response to the increasing frequency and severity of cardiovascular disease and cancer. The cardio-oncology care team provides comprehensive support to patients throughout the entire survivorship process, from the initial cancer diagnosis to post-treatment care. To enhance the quality of cardiovascular treatment for cancer patients, it is imperative to augment the number of cardiologists trained to address the escalating number of cancer patients (Koutsoukis et al., 2018).

Cardio-oncology, a relatively recent subspecialty of cardiology, is the medical specialty concerned with the treatment of cardiovascular conditions in patients with cancer. The fundamental paradigm of cardio-oncology is the prevention, diagnosis, and treatment of cardiotoxicity resulting from radiation and chemotherapy. An illustration of a "less classical" cardio-oncology objective would encompass the detection and treatment of cardiac amyloidosis, primary and metastatic cardiac tumors, and other related conditions (Li et al., 2023).

The occurrence of cardiotoxicity is contingent upon the specific treatment modality employed. In 3-26% of patients treated with doxorubicin, 2-28% with trastuzumab, and 2.7-11% with sunitinib, cardiotoxicity manifests as an adverse event. A recent retrospective analysis revealed that 6.6% of patients undergoing chemotherapy for breast or hemostatic cancer experienced heart failure. Furthermore, an increased prevalence of arrhythmia, thromboembolism, and coronary artery disease has been observed in cancer patients. Coronary artery disease (CAD) and cancer have been shown to share similarities in their risk factor profiles and genetic and physiological mechanisms (Li et al., 2023).

Biomarkers in Cardio-Oncology

Cardiac damage and inflammation are examples of cardiotoxicities that have been identified using a variety of biomarkers. Cardiotropin (cTn), natriuretic peptides (NP), interleukin-6 (IL-6), and C-reactive protein have been identified as useful markers for myocardial damage and cardiac insufficiency in the early stages of treatment. In addition, proteomics, genome-wide association studies, and microRNAs are being investigated for the purpose of identifying novel indicators of inflammation or cardiovascular injury. Myocarditis, a potential complication of immune checkpoint inhibitor (ICI) therapy during tumor treatment, has been identified through the assessment of soluble suppression of tumorigenicity-2 (sST2) levels (Hayek et al., 2019).

Cardiovascular Complications Caused by Chemo-Radiotherapy

Coronary artery disease, systolic and diastolic heart dysfunction, pulmonary and arterial hypertension, supraventricular and ventricular arrhythmias, and other major cardiovascular side effects have been associated with anti-cancer medication. The cardiovascular complications observed may be partially attributed to endothelial dysfunction, thrombogenesis, and myocardial damage, which are known adverse effects of chemotherapy and radiotherapy (Li et al., 2023).

Cardiotoxicity Caused by Chemotherapy

Cancer treatment-induced cardiac dysfunction is broadly classified into two distinct categories: type I and type II cardiotoxicity. This classification is based on the nature of myocardial injury, its reversibility, and its relationship to drug dosage. Type I cardiotoxicity is characterized by direct myocardial cell damage, often leading to irreversible cardiac dysfunction (Huang et al., 2022). A notable example is anthracycline-induced cardiotoxicity, which is dose-dependent and associated with progressive myocardial injury, increasing the risk of heart failure even years after treatment (Abdul-Rahman et al., 2023; Li et al., 2023; Tetterton-Kellner et al., 2024). Conversely, type II cardiotoxicity is generally reversible and arises from impaired myocardial cell function rather than cell death. Trastuzumab-induced cardiotoxicity is a well-known example of this phenomenon, wherein cardiac dysfunction occurs independently of the cumulative dose and often improves after the discontinuation of the drug (Li et al., 2023). Despite the fact that these two forms of cardiotoxicity possess distinct mechanisms, they frequently overlap, particularly in patients receiving both anthracyclines and trastuzumab, which can lead to an increased risk of cardiac dysfunction. It is imperative to comprehend these discrepancies to enhance cancer treatment while reducing the incidence of long-term cardiovascular complications (Hayek et al., 2019).

Radiotherapy Causes Cardiotoxicity

The assessment of the relative risk of developing heart failure during radiation treatment is complicated by the frequent administration of cardiotoxic chemotherapy in conjunction with radiation therapy. The risk of cardiotoxicity is higher in breast cancer patients treated with a combination of chemotherapy and radiation compared to those treated with chemotherapy alone. It is important to note that radiation exposure and the onset of clinically noticeable cardiac failure may occur at different times. The extant literature describes the development of substantial fibrosis following radiation therapy, which has the potential to impact all cardiac components, including the myocardium, pericardium, coronary arteries, and

heart valves. It is noteworthy that patients receiving radiotherapy to chest may induce coronary, myocardial or valvular heart disease after prolonged treatment (Abdul-Rahman et al., 2023; Li et al., 2023; Tetterton-Kellner et al., 2024).

Monitoring Cardiotoxicity

Chemotherapy

Future cardiotoxicity evaluation strategies will involve the systematic and integrated use of both established and emerging imaging modalities, such as electrocardiograms (ECGs), circulating biomarkers, cardiac MRI, and speckle-tracking imaging. The invasiveness of the endomyocardial biopsy precludes its use as a screening tool, despite its status as the most sensitive and specific method for evaluating cardiac injury. The procedure is reserved for rare instances in which cardiac dysfunction is not evidently linked to chemotherapy (Ganatra et al., 2020; Pizzino et al., 2014).

Radiotherapy

According to the consensus statements, screening for cardiovascular (CV) disease should be performed even in asymptomatic survivors, given the elevated risk of CV consequences. Subsequent to a period of 5-10 years post-radiation therapy (RT), and subsequently every 5 years thereafter, unless there is the manifestation of concerning symptoms in the interim, a functional non-invasive stress test and echocardiography are recommended. At our institution, the preferred methods for the screening of radiation-induced coronary disease are coronary computed tomography (CT) coronary calcium scoring and stress echocardiography. The issue of radiation exposure represents a significant concern in the context of radio-nuclide imaging, a diagnostic modality that utilizes either positron emission tomography (PET) or single-photon emission computed tomography (SPECT) to identify cases of coronary artery disease (CAD). However, it is important to note that the diagnostic sensitivity and specificity of radio-nuclide imaging are comparable to those of echocardiography (Narowska et al., 2023).

Conclusion

Cardio-oncology signifies a pivotal nexus between cardiovascular health and cancer care, addressing the mounting challenge of cardiotoxicity induced by chemotherapy and radiotherapy. As cancer treatments continue to advance, the risk of cardiovascular complications necessitates early detection, comprehensive monitoring, and effective management strategies. Biomarkers, advanced imaging modalities, and multidisciplinary collaboration play pivotal roles in mitigating these risks, ensuring better outcomes for cancer patients. A robust collaboration between the oncology/hematology team and the cardiology/cardio-oncology services is imperative for enhancing patient outcomes. The importance of screening and early referral by the oncology team cannot be overstated. Furthermore, there is a necessity for heightened awareness and the augmentation of cardio-oncology services and training to enhance patient outcomes. Integration of cardioprotective measures into oncology protocols is a strategy that healthcare providers can implement to optimize both cancer survival and long-term cardiovascular health. Continued research and innovation in this field will further refine preventive strategies, ultimately improving the quality of life for cancer survivors.

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