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Review

Cardiotoxicity and Chemotherapy-Induced Hormonal Homeostatic Imbalance: A Review Article

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ABSTRACT

Chemotherapy-induced cardiotoxicity represents a major complication in the care of cancer patients, presenting as systolic ventricular dysfunction, arrhythmias and myocardial ischemia. While modern chemotherapy regimens have improved survival rates, cardiovascular adverse effects may compromise prognosis and quality of life. Definitions of cardiotoxicity vary but often rely on a ≥10% reduction in left ventricular ejection fraction (LVEF) or a drop below 53%. Classically, cardiotoxicity is categorized as acute (within 14 days of treatment), subacute (during treatment) and late (after one year), with late toxicity being the most prevalent and often irreversible. Key agents include anthracyclines, with a cumulative risk of cardiac dysfunction ranging from 5% to 25% depending on the total dose; anti-HER2 antibodies, which are generally reversible; fluoropyrimidines, linked to coronary vasospasm; taxanes, which induce arrhythmias; and tyrosine kinase inhibitors, with a broad spectrum of ventricular damage and hypertension. The pathophysiology involves free radical generation, myocardial DNA damage, mitochondrial dysfunction and blockade of the neuregulin/HER signaling pathway. Early detection relies on high-sensitivity biomarkers and echocardiography with longitudinal strain, essential to prevent irreversible progression. Guidelines recommend baseline cardiovascular evaluation, periodic monitoring and prophylactic use of beta-blockers and ACE inhibitors in cases of subclinical decline. Management includes discontinuation or modification of treatment, cardioprotective drugs and cautious reintroduction, balancing risks and benefits. In conclusion, integrated collaboration between oncologists and cardiologists is vital to optimize antineoplastic therapy, minimize cardiovascular morbidity and ensure better long-term outcomes, making early monitoring a fundamental pillar in modern cancer care.

Keywords: Cardiotoxicity; Chemotherapy; Left ventricular ejection fraction; Anthracyclines; Cardio-Oncology

Introduction

Recent advances in oncology, particularly the development of highly effective chemotherapeutic agents, have significantly increased cancer patient survival. However, there has been a growing incidence of cardiovascular complications during and after treatment, representing a new clinical and scientific challenge: chemotherapy-induced cardiotoxicity. This condition is characterized by changes in cardiac structure and function resulting from the direct or indirect effects of chemotherapeutic agents, potentially manifesting as systolic ventricular

dysfunction, myocardial ischemia, arrhythmias, pericarditis, myocarditis and hypertension. Although anthracyclines remain a cornerstone in the treatment of several tumours, their mechanism of free radical generation and interference with topoisomerase II-β results in mitochondrial damage and cellular apoptosis, with a cumulative risk of dysfunction exceeding 20% at doses above 400 mg/m².

Beyond cardiac effects, chemotherapeutic agents can also disrupt hormonal balance by altering the function of glands such as the thyroid, adrenal glands and gonadal axis, justifying a multidisciplinary approach involving both cardiology and endocrinology in oncologic practice. In comparison, targeted therapies such as trastuzumab present functional cardiotoxicity through inhibition of the neuregulin/HER2 pathway, though reversible in most cases with appropriate cardiovascular measures. Fluoropyrimidines are notably associated with coronary vasospasm and acute ischemia, while taxanes and tyrosine kinase inhibitors broaden the range of adverse manifestations. Consequently, early detection of subclinical changes using biomarkers and advanced imaging techniques becomes imperative for preserving cardiac function.

Objectives

This study aims to characterize the definitions, classifications and mechanisms of chemotherapy-induced cardiotoxicity; identify risk factors associated with cardiac dysfunction in cancer patients; and assess strategies for early detection, prevention and management of this adverse event.

Materials and Methods

A narrative review of the scientific literature was conducted from January to March 2025 using the PubMed, SciELO, Google Scholar and ScienceDirect databases. Keywords included "cardiotoxicity," "chemotherapy," "left ventricular ejection fraction," "cardiac biomarkers," and "cancer treatment." Articles published in the last ten years with proven clinical relevance were included, while case reports and non-peer-reviewed publications were excluded.

Discussion

The reviewed studies first highlight the heterogeneity in definitions of chemotherapy-induced cardiotoxicity, which hampers comparison between studies and standardization of clinical protocols. Spinelli, et al.[1] classify toxicity into three severity grades based on changes in LVEF, while Medeiros and Wiehe adopt a ≥10% reduction in LVEF to a final value below 53% as a diagnostic threshold, emphasizing the predictive role of longitudinal strain detected by speckle-tracking echocardiography. This discrepancy underscores the need for international consensus to standardize criteria and enable robust meta-analyses. Regarding pathophysiological mechanisms, Pinto, et al.[2] describe how anthracyclines induce mitochondrial damage and apoptosis via reactive oxygen species and inhibition of topoisomerase II-β in cardiomyocytes. In contrast, trastuzumab blocks the neuregulin/HER2 survival pathway and typically leads to reversible ventricular dysfunction if cardioprotective measures are promptly applied[3]. The distinction between type I (irreversible) and type II (generally reversible) toxicity is crucial for therapeutic decision-making, such as cautious reintroduction of trastuzumab after LVEF recovery.

Fluoropyrimidines exhibit a unique profile, with coronary vasospasm and acute ischemia incidence ranging from 1% to 18% depending on regimen and combination with other cytotoxic agents[2]. This phenomenon results from endothelial damage and activation of prothrombotic pathways, requiring continuous ECG monitoring and immediate drug withdrawal at the first ischemic sign. Taxanes and tyrosine kinase inhibitors exhibit more diverse toxicities, including arrhythmias and systemic hypertension, significantly increasing the risk of severe adverse events, particularly in patients with prior cardiovascular risk factors such as coronary disease or thoracic radiotherapy[3].

Another relevant point is the early detection of subclinical cardiotoxicity. Boas, et al. report that elevations in high-sensitivity troponin and 10-15% reductions in global longitudinal strain precede LVEF decline, creating a therapeutic window for introducing β-blockers and ACE inhibitors before symptomatic impairment occurs[4]. This finding supports the routine inclusion of combined biomarker and imaging protocols, especially in high-risk patients. Pharmacological prophylaxis has also gained momentum. Spinelli, et al. and Medeiros and Wiehe report that prior use of β-blockers and aldosterone antagonists reduces the incidence of ventricular dysfunction[1,3], while Pinto, et al. describe LVEF improvements of up to 10% when these drugs are introduced at the first sign of subclinical decline[2]. These findings support guidelines recommending cardioprotective therapy initiation in patients showing elevated troponin or reduced strain in the absence of clinical symptoms.

The implementation of integrated Cardio-Oncology units, as described by Boas, et al.[4], has demonstrated a positive impact on cardiovascular outcomes without compromising cancer control. In these multidisciplinary teams, oncologists, cardiologists, nurses and imaging specialists collaborate to adjust dosages, modify regimens and optimize interventions, resulting in fewer heart failure admissions and maintenance of effective anticancer therapy[5-9]. However, important gaps remain, such as the lack of randomized prospective trials comparing different surveillance and cardioprotective strategies, as well as studies exploring new biomarkers and noninvasive imaging techniques[10,11]. There is also a lack of data in specific populations, including the elderly, pediatric patients and individuals with pre-existing cardiovascular disease. Overall, the current body of evidence highlights three key pillars for mitigating chemotherapy-induced cardiotoxicity: (1) standardization of diagnostic criteria; (2) early surveillance using biomarkers and advanced imaging; and (3) pharmacological prophylaxis and multidisciplinary management in Cardio-Oncology units. The integration of these elements may significantly improve event-free survival and quality of life in patients undergoing chemotherapy[12,13]. Although the literature mainly focuses on cardiac dysfunction, there is growing evidence that chemotherapy also affects the endocrine axis, with reports of hypogonadism, subclinical hypothyroidism and alterations in the hypothalamic-pituitary axis. These effects, although less documented, may negatively impact metabolism, mood and quality of life, warranting periodic hormonal evaluations in integrated surveillance protocols[14,15].

Conclusion

Chemotherapy-associated cardiotoxicity has emerged as a central challenge at the intersection of oncology and cardiology, requiring a careful balance between antitumor efficacy and

cardiac function preservation. The variability in diagnostic criteria highlights the need for unified standards to support clinical decision-making and comparative research. Moreover, further studies are needed to investigate the hormonal impacts of chemotherapy in greater depth, advocating for multidisciplinary care protocols that also involve endocrinologists. Finally, the consolidation of Cardio-Oncology units with multidisciplinary collaboration is essential for optimizing cardiovascular outcomes without compromising anticancer effectiveness.

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