REVIEW

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Cardiac Toxicity of Cancer Therapies: Mechanisms, Surveillance, and Clinical Implications

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Abstract

Cardiotoxicity caused by cancer treatments is a growing concern as the survival rate of cancer increases. This review synthesizes the current research on cancer therapy-related cardiac toxicity. A comprehensive literature search was performed in PubMed, Scopus, and Google Scholar (2015-2025). Chemotherapy drugs like anthracyclines cause irreversible myocardial injury via oxidative stress and mitochondrial dysfunction, while trastuzumab causes reversible dysfunction through human epidermal growth factor receptor 2 (HER2) signaling disruption. Radiation can lead to heart disease years later, and immunotherapy sometimes triggers heart inflammation. Surveillance relies on advanced imaging (e.g., global longitudinal strain echocardiography, cardiac magnetic resonance imaging) and biomarkers (troponin, B-type natriuretic peptide), though guidelines from American Society for Clinical Oncology and European Society of Cardiology differ in monitoring frequency and biomarker use. Risk stratification is essential, with high-dose anthracyclines, prior cardiovascular disease, and HER2-targeted therapies posing elevated risks. Primary prevention strategies include dexrazoxane and sodium-glucose cotransporter 2 inhibitors. Secondary prevention uses heart failure therapies. New tools; like artificial intelligence and genetic testing, may soon predict who is at risk and guide personalized care. By balancing cancer treatment success with heart safety, we can improve long-term health for survivors.

Keywords: Cardiotoxicity, cancer therapy, chemotherapy, radiation therapy, heart failure, anthracyclines

INTRODUCTION

Cardiotoxicity refers to a substance's harmful effects on the heart, which can result in cardiomyopathy, heart failure (HF), or a significant reduction in the left ventricular ejection fraction (LVEF).[1] HF, coronary artery disease (CAD), arrhythmias, QT prolongation, arterial hypertension, and peripheral vascular disease are among the cardiovascular (CV) problems that may arise from cancer treatment. Even if the morbidity and mortality of cancer have significantly decreased as a result of early detection and treatment, some of the more recent anti-cancer signaling inhibitors and traditional chemotherapeutics may have CV side effects that affect a patient's quality of life and survival.[2,3] Cardiotoxicity was categorized as mild, moderate, or severe based on the degree of myocardial damage or dysfunction seen in patients during follow-up.[4]

According to 2022 estimates, approximately 20 million individuals were newly diagnosed with cancer globally, and 9.7 million people died from the disease. Around 53.5 million people were living within five years of a cancer diagnosis, reflecting a growing global survivor population. It is estimated that 1 in 5 people will be diagnosed with cancer during their lifetime, with 1 in 9 men and 1 in 12 women dying from it.[5] In the United States, as of January 1, 2025, approximately 1 in every 18 Americans (18.6 million people)

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was a cancer survivor, a number projected to exceed 22 million by 2035.[6] The discovery of cancer drugs is advancing at a rapid pace, and survival rates are rising. We should focus on preventive strategies and on addressing the CV risks of cancer therapy.[7]

Based on a cohort study of 36,232 adult cancer survivors, ischemic heart disease, stroke, and cardiomyopathy and HF were prevalent in those with significant CV risk factors. Overall, cancer survivors with CVD had a 60% survival rate, while those without CVD had an 81% survival rate ($P < 0.01$).[8] Similarly, a 2019 systematic review (21 studies through 2018) reported that cancer therapy-related cardiac dysfunction (CTRCD) occurred in 9.3-43.8% of patients (pooled incidence ≈21%).[9]

Cardiotoxicity risk and outcomes vary substantially by race and ethnicity. For instance, Black cancer patients have been shown to have approximately 71% higher odds of developing chemotherapy-associated cardiotoxicity than White patients.[10] In a multiracial cohort of patients receiving anthracycline-based chemotherapy, non-Hispanic (NH) Black, Hispanic, and Asian individuals had a significantly higher incidence of cardiotoxicity (16.3%, 14.7%, and 18.2%, respectively), compared to NH White patients (7.2%). Even after adjusting for comorbidities, socioeconomic status, anthracycline dose, and baseline LVEF, NH Black and Hispanic individuals had independently increased risks, with hazard ratios of 2.62 and 2.37, respectively.[11]

Cardio-oncology (CO) is a field that has emerged to assist cancer patients in preventing, managing, and reducing CV disorders, as well as to help weigh the benefits and drawbacks of cancer therapies. Helping patients comprehend the trade-offs between oncologic efficacy and CV risks is crucial.[12]

Aim

This review aims to highlight the growing significance of CO in reducing CV risks among cancer survivors and guiding the creation of holistic, multidisciplinary treatment approaches that maximize CV safety and oncologic efficacy by analyzing the available data. Also, it is important to examine the mechanisms, classification, clinical implications, outcomes, and prevention of cancer-related thrombosis-central venous thrombosis, given its importance in medical practice and research.

Section 1: Literature Search Strategy

A comprehensive search of PubMed, Scopus, and Google Scholar (January 2015-May 2025) was performed. We also added some essential publications that are not within this time frame. Relevant publications were identified using key terms "cardiotoxicity", "cancer therapy", "chemotherapy", "CO", "CTRCD", "CV complications", "HF", "cardiotoxicity outcomes", and "human epidermal growth factor receptor 2 (HER2) inhibition HF". All original research and review articles written in English that involved human or relevant animal models were included.

Section 2: Classification

As is well established, chemotherapy or other concomitant cancer treatments affect the CV system. Delayed cardiotoxic effects, such as those associated with anthracyclines, can manifest many years after therapy, suggesting that patients require long-term vigilance.[13] For example, anthracycline-induced cardiomyopathy may not appear until decades posttherapy,[14] and current guidelines, therefore, recommend extended cardiac monitoring for survivors of anthracycline treatment.[15] The clinical management of these effects follows a specific approach that coordinates time, reversibility, and damage presentation, enabling reasonable anticipation. Cardiac damage is usually classified according to its clinical course as acute or chronic, and either reversible or irreversible, subclinical or symptomatic.

Acute Cardiotoxicity

Acute cardiotoxicity describes heart injury sustained during cancer treatment or within several weeks after treatment. It typically arises rapidly (often within days of therapy) and is usually transient, often reversing after the drug is stopped or with prompt cardiac support.[14] Distinctive features include arrhythmias, pericarditis, or severe left ventricle (LV) systolic dysfunction.[16,17]

Chronic Cardiotoxicity

Chronic cardiotoxicity is described as occurring months to years after the treatment has been completed. It is the consequence of cumulative myocardial injury, which is frequently caused by anthracyclines and trastuzumab.[18,19] As an example, the clinically unnoticeable stages of doxorubicin (DOX)-induced damage can last for years until it manifests as chronic HF, which, depending on dosage and several risk factors, occurs in around 5%-45% of patients.[13,19] Generally, trastuzumab toxicity is less severe, but it can be observed after anthracycline treatment.[19]

Reversible vs. Irreversible Cardiotoxicity

Reversibility is a key factor in assessing cardiac harm. Trastuzumab's effects, such as dysfunction, are generally reversible, and they will resolve after cessation of the drug. Conversely, damage caused by anthracyclines is usually irreversible due to oxidative damage and myocyte death, potentially leading to chronic HF.[20] Knowing these types, helps in deciding whether to suspend therapy or to employ protective measures with angiotensin converting enzyme (ACE) inhibitors and beta-blockers.[20]

Subclinical vs. Symptomatic Cardiotoxicity

Subclinical cardiotoxicity is characterized by the absence of symptoms and the presence of myocardial dysfunction, and it is possible to identify it through speckle-tracking echocardiography. A greater than 15% reduction in global longitudinal strain (GLS) is an indication of early dysfunction, indicated by preserved echocardiographic measures.[21,22] Symptomatic cardiotoxicity manifests as fatigue, dyspnea, and signs of HF. Early detection of subclinical changes helps prevent long-term damage.[23]

Section 3: Mechanisms of Cardiotoxicity

Cancer therapies cause cardiotoxicity via distinct mechanisms: type I (irreversible) from cytokines and type II (reversible).[24] This section discusses several mechanisms associated with cancer therapies:

Chemotherapy

Anthracyclines such as epirubicin, DOX, and daunorubicin are commonly used to treat solid and hematologic cancers. Nevertheless, disruption of sarcomeres, the production of cardiotoxic anthracycline metabolites, the production of reactive oxygen species (ROS) through inhibition of topoisomerase 2β (which triggers cell death pathways and mitochondrial dysfunction), and their transport across the cardiomyocyte membrane may all be contributors to cardiomyocyte damage.[2] Reduced ferritin and increased labile iron result from DOX's disruption of ferritin's IRE. This results in damage to the heart muscle and an increase in ROS. Receptor-interacting serine/threonine-protein kinase 3 is upregulated by DOX. DOX binds and phosphorylates calmodulin kinase II and controls the opening of the mitochondrial permeability transition pore, which causes necroptosis and apoptosis. Deactivating the Top2β gene in mice's hearts reduces DOX-induced cardiac failure, as DOX inhibition of the gene causes ROS buildup, RCD pathway activation, and mitochondrial malfunction.[25-27]

Targeted Therapy

Tumor-targeted agents such as immune checkpoint inhibitors (ICIs), protein kinase inhibitors, and vascular endothelial growth factor inhibitors each carry distinct cardiotoxic risks. Trastuzumab, an anti-HER2 antibody that has markedly improved survival in HER2-positive breast cancer, can disrupt cardiac Erb-B2 receptor tyrosine kinase 2 (ERBB2)/ERBB3 signaling by binding domain IV of the ERBB2 receptor on cardiomyocytes. This interference impairs the heart's stress response, leading to apoptosis, inflammation, microvascular injury, oxidative stress, and interstitial fibrosis.[28-30] Inhibiting neuregulin-1 / HER2 and angiotensin II/AT1 pathways further increases ROS, sensitizing myocytes to additional insults. When given with anthracyclines like DOX, trastuzumab exacerbates Top2B inhibition, accelerating apoptosis and oxidative/nitrative damage; thus, avoiding simultaneous administration reduces heartfailure risk.[28-30]

Proteasome inhibitors (e.g., carfilzomib, bortezomib) induce cardiotoxicity primarily via mitochondrial dysfunction and proteasome overload, triggering apoptosis in cardiomyocytes.[30,31] Notably, the degree of LVEF decline predicts trastuzumab-induced cardiotoxicity (hazard ratio: 2.4; 95% confidence interval: 1.2-6.03; $P = 0.049$), and in 86% of affected patients, dysfunction is eventually reversible.[32]

Radiation Therapy

Radiation induces oxidative stress and chronic inflammation, leading to endothelial dysfunction, leukocyte extravasation, vasodilation, increased permeability, and excessive eicosanoid synthesis. Overproduction of ROS, altered calcium homeostasis, and upregulated nicotinamide adenine dinucleotide phosphate oxidases damage the myocardial capillary network, causing ischemia, cardiomyocyte apoptosis, and fibrosis.[33-37] Ionizing radiation also injures coronary arteries and accelerates atherosclerosis; irreversible DNA damage occurs when intracellular antioxidants are overwhelmed, and suppression of antioxidant enzymes further increases ROS accumulation.[38,39] Ultimately, these processes promote premature CAD in irradiated patients.

Immunotherapy

Cancer immunotherapies, active and passive, include cytokines, monoclonal antibodies, checkpoint inhibitors (e.g., nivolumab, pembrolizumab, ipilimumab), and bispecific T cell engagers. ICIs block cytotoxic T lymphocyte antigen 4 (CTLA-4) and programmed cell death 1 or its ligand, unleashing T cell activity against tumors but risking autoimmunity. When checkpoints are inhibited, T cells may attack endothelial cells (causing atherosclerosis or vasculitis) or cardiac / myocardial cells (leading to myocarditis or pericarditis).[40-42] Murine models show that CTLA-4 blockade alone can precipitate myocarditis, and in humans, shared antigens between tumor cells and cardiomyocytes can drive T cell-mediated myocardial infiltration, arrhythmias, and HF.[43-45] The mechanisms of cardiotoxicity from various cancer therapies are summarized in Table 1.

Section 4: Surveillance and Diagnostic Criteria

For accurate diagnosis of the cardiotoxicity of cancer therapies, several imaging techniques and certain biomarkers are used. Risk stratification guides tailored surveillance and management.

Table 1. Definitions and mechanisms of major cancer therapy-induced cardiotoxicities

Agent	Mechanism	Onset	Reversibility	Detection modality	Reference
Anthracyclines	Dose-related myocardial injury via ROS	Acute-chronic (weeks-years)	Often irreversible	LVEF decline on echocardiogram	[2,13,20,25-27,46,47]
HER2-targeted therapy	Inhibition of ERBB2 signalling ↓ in myocyte repair	Early (<6 mo)	Generally reversible	GLS by speckle-tracking echo	[19-22,28-30]
Tyrosine kinase inhibitors	Vascular/endothelial toxicity	Variable (weeks-months)	Variable	Blood pressure, biomarkers	[30,31,52]

↓: Indicates inhibition or downregulation, HER2: Human epidermal growth factor receptor 2, ROS: Reactive oxygen species, LVEF: Left ventricular ejection fraction, GLS: Global longitudinal strain, ERBB2: Erb-B2 receptor tyrosine kinase 2

Imaging

Echocardiography has emerged as an important tool in the diagnosis of cardiotoxicity due to cancer therapies.[46] LVEF is used to detect cardiac dysfunction and remains the mainstay to determine further management of a patient with cardiac dysfunction.[47] LVEF is not very sensitive when it comes to the detection of minute changes in LV function. Cardiotoxicity, characterized by a decrease in LVEF or HF, seems to be best predicted by a 10% to 15% reduction in GLS measured by speckle tracking echocardiography early during therapy. Global radial and circumferential strain measurements are routinely abnormal in late cancer survivors, even when LVEF is normal. However, their therapeutic utility in predicting eventual HF or ventricular dysfunction has not been investigated.[48] The routine imaging modality by which LVEF is determined is 2-dimensional (2D) echocardiography.[47] Small changes in LV contractility are also often overlooked and not detected in calculated 2D LVEF.[46] This loophole can be overcome by implementing stricter regulatory measures.

Over the last decade or so, the evaluation of GLS from speckle-tracking analysis of 2D echocardiography has become a practical and better replacement for LVEF for assessing myocardial function.[47] While 3D echocardiography provides increased precision and robustness, its accessibility is not widespread.[49] The American Society for Clinical Oncology (ASCO) endorses the determination of GLS to be conducted in cancer patients undergoing cardiotoxic therapies.[47] Guidelines direct us to compare the GLS values measured while on chemotherapy with baseline GLS values. A reduction of >15% compared to baseline is considered to be worrisome. A decrease in GLS compared to baseline or a low total GLS value during initial chemotherapy is a sign of an individual who is at high risk of developing chemotherapy-related cardiac dysfunction (CTCRD).[9,46]

Cardiac magnetic resonance (CMR) is the gold standard for detecting edema and fibrosis via T2-weighted short tau inversion recovery and late gadolinium enhancement, and also measuring ventricular volumes and function.[50,51] Additionally, Myocardial T1 mapping employs T1 relaxation times to determine the volume of distribution of gadolinium-based contrast agents, which are used to determine diffuse myocardial fibrosis, in the myocardium. Numerous CMR-based clinical studies have utilized T1 measurements and mapping to examine myocardial remodeling in cancer patients and survivors.[49] Several biomarkers have also been explored, studied, and tested as an alternative to or addition of imaging techniques for the assessment and management of cardiotoxicity.[40]

Biomarkers

High-sensitivity troponin and natriuretic peptide [B-type natriuretic peptide (BNP), N-terminal pro-BNP (NT-proBNP)] are recommended for early detection and risk stratification in CTCRD (class 1A). Although the specificity of BNP is still debated as it can also be increased without clinical HF, during severe sepsis and septic shock, and has a positive correlation with high sensitivity C-reactive protein (CRP), therefore, its specificity is still questioned.[52] Cardiotoxicity is the main cause of mortality in cancer survivors, after the cancer itself resolves.[53] Table 2 summarizes the modalities and biomarkers.

ASCO/ESC Guidelines for Risk Stratification and Monitoring

CV risk should be stratified based on the level of risk associated with the specific anti-cancer therapy being used, and each patient's CV disease history and risk factors. These suggestions are included in both sets of guidelines. Additionally, the European Society of Cardiology (ESC) guidelines suggest monitoring with 2D transthoracic echocardiography at baseline and every 3 months during anti-HER2 therapy in every single patient, regardless of risk. On the other hand, the prior ASCO guidelines suggest screening only in high-risk patients, and that the physician determines, the frequency based on clinical judgement and patient circumstances.[48] Regarding biomarkers, the ESC guidelines have a recommendation distinct from that of ASCO. According to the ESC, patients who have had prior anthracycline therapy should have their blood cardiac troponins and natriuretic peptides monitored.[54] ASCO states

Table 2: Surveillance modalities and biomarkers

Modality / Biomarker	Utility	Notes	Reference
2D Echocardiography (LVEF)	LV dysfunction detection	Insensitive to small changes	[46,47]
Speckle-Tracking Echocardiography (GLS)	Early dysfunction (≥15% reduction)	Recommended by ASCO; high sensitivity	[21,22,47,48]
3D Echocardiography	Improved precision	Limited accessibility	[49]
Cardiac MRI (T2-STIR, LGE, T1 mapping)	Edema, fibrosis, volumes	Gold standard for tissue characterization	[50,51]
High-sensitivity Troponin	Early myocardial injury	High sensitivity; specificity caveats	[52]
BNP / NT-proBNP	Heart failure risk stratification	Elevated in HF, sepsis; correlates with CRP	[52]

≥: Indicates greater than or equal to, 2D: 2-dimensional, LVEF: Left ventricular ejection fraction, GLS: Global longitudinal strain, T2-STIR: T2-weighted short tau inversion recovery, LGE: Late gadolinium enhancemen, MRI: Magnetic resonance imaging, BNP: ASCO: American Society for Clinical Oncology, HF: Heart failure, CRP: C-reactive protein

that there is still a need for further studies to clarify the role of biomarker assessment during cancer therapy.[8] (See Table 3 for a summary of ASCO vs. ESC guideline recommendations) Additionally, regarding risk stratification, patients who have been treated with high-dose anthracyclines (eg, DOX ≥250 mg/m^2), or low-dose anthracyclines (eg, DOX <250 mg/m^2), in the presence of several CV risk factors like smoking, hypertension, diabetes, dyslipidemia, obesity and compromised cardiac function (low LVEF) are considered to be at an increased risk for developing cardiac toxicity.[8,55,56]

Section 5: Clinical Manifestations and Outcomes

Acute / Early Effects

Cardiac toxicity can manifest during or shortly after treatment. For example, ICIs (e.g., nivolumab, pembrolizumab) can trigger fulminant autoimmune myocarditis, typically presenting early in therapy (median ~34 days).[57-59] Though rare (≈1% incidence), ICI myocarditis carries high mortality (~40-50%). Symptoms often include acute HF and life-threatening arrhythmias. Fluoropyrimidines [5-fluorouracil (5-FU)/capecitabine] classically cause coronary vasospasm and ischemia, leading to anginal chest pain and electrocardiography (ECG) changes mimicking acute coronary syndrome,[57] Acute toxicities may present as:

- Chest pain (angina): Often due to 5-FU-induced coronary vasospasm.[57]
- Palpitations/arrhythmias: Atrial fibrillation (~30%) and ventricular tachyarrhythmias (~27%) have been reported in ICI myocarditis.[58]
- Dyspnea: From acute HF or pulmonary edema (noted in ~5% of 5-FU cases.[57]
- Other signs: Rarely, 5-FU can cause pericarditis (≈1-2% of cases[57]) or mimic acute coronary syndrome on ECG; ICI myocarditis can also present with complete heart block or cardiogenic shock.[58]

Immediate recognition is critical. ICI myocarditis often requires prompt high-dose corticosteroids (per expert guidance), and 5-FU cardiotoxicity may require anti-anginal therapy (nitrates, calcium channel blockers) and discontinuation of the agent.[57,59]

Chronic / Late Effects

Dilated cardiomyopathy and chronic HF typically emerge months to years after treatment.[60] Anthracyclines (e.g., DOX) cause dose-related myocardial injury that usually presents late. Trastuzumab (HER2 therapy) cardiomyopathy often appears

Table 3: Guidelines recommend tailored surveillance based on risk stratification

Parameter	ASCO guidelines (2017)	ESC guidelines (2022)	Reference
Baseline assessment	LVEF, GLS, Troponin	LVEF, GLS, troponin, BNP/NT- proBNP	[8,54]
High-risk patients	Anthracycline ≥ 250 mg/m^2 + CV risk factors	Prior CVD, radiation ≥30 Gy, HER2- targeted therapy	[8,54]
Imaging frequency	Every 3-6 months during therapy	Every three months during anti-HER2 therapy	[8,54]
Biomarkers	Insufficient evidence for routine use	Troponin / BNP monitoring post - anthracycline	[8,54]
Intervention	Start HF therapy if LVEF drops ≥10% or GLS >15%	ACE inhibitors/beta-blockers for LVEF ≤ 50%	[8,54]

ASCO: American Society for Clinical Oncology, ESC: European Society of Cardiology, LVEF: Left ventricular ejection fraction, GLS: Global longitudinal strain, BNP: B-type natriuretic peptide, NT-proBNP: N-terminal pro-B-type natriuretic peptide, CV: Cardiovascular, ACE: Angiotensin converting enzyme, HER2: Human epidermal growth factor receptor 2

during therapy or within the first year and can improve with treatment interruption.[60] Patients may have no early symptoms; later, they develop classic HF. Symptoms of chronic cardiotoxicity include:

• Fatigue and exercise intolerance (reduced activity tolerance), the most common early complaints of HF.

• Conditions such as dyspnea on exertion, orthopnea, and paroxysmal nocturnal dyspnea (shortness of breath on exertion or lying flat) are important considerations in patient assessment.

• Peripheral edema and weight gain (ankle/leg swelling, bloating).

• Persistent cough or wheezing (due to pulmonary congestion).

Patients developing late cardiotoxicity often have a severely impaired prognosis.[60] Some improve substantially with standard HF therapy (ACE inhibitors, beta-blockers, etc.) For example, one series showed recovery of function in many patients if treated early.[61] However, others progress to chronic HF requiring lifelong management. The data on outcomes data suggest a worse prognosis for those with cancer therapy-related cardiomyopathy: "patients experiencing cardiotoxicity develop HF months to years after therapy, and have a severely impaired CV prognosis."[60]

Disparities: Notably, some populations show higher late cardiotoxicity rates. For example, Black women on HER2-targeted breast cancer therapy had significantly higher 1-year cardiotoxicity incidence (24%) than White women (7%).[62] This suggests enhanced surveillance may be warranted in higher-risk groups.

Outcomes: Many patients respond to guideline-directed HF therapies.[61] However, persistent dysfunction can still lead to morbidity and mortality. Even "recovered" patients remain at risk for recurrence of dysfunction. ICI myocarditis mortality has been reported around 40-50%.[59] Long-term follow-up with routine echocardiography, ECGs, and biomarkers (troponin, BNP) in collaboration with CO is recommended for all survivors.[60]

Section 6: Management and Prevention

Standard chemotherapeutic treatments as well as targeted treatments are associated with a greater risk of heart damage, such as HF and LV dysfunction. High doses of DOX and other anthracyclines are said to increase the risk of HF. However, studies have shown that therapies such as dexrazoxane, ACE inhibitors, sodium-glucose cotransporter 2 (SGLT2) inhibitors, and early detection of LV dysfunction can effectively reduce anthracycline-induced toxicity while preserving chemotherapy efficacy.[63]

Primary Prevention

Numerous medications have been investigated for their possible cardioprotective benefits during cancer treatment. Primary prevention includes dexrazoxane (10 mg/m^2 per 1 mg/m^2 DOX), and emerging agents such as SGLT2 inhibitors. Dexrazoxane is food and drug administration approved for anthracycline cardioprotection, though its use is debated (concerns include potential interference with chemotherapy efficacy and reported secondary malignancy risk in pediatric studies). SGLT2 inhibitors, which reduce oxidative stress and inflammation,[64-68] now have a class I recommendation in HF guidelines.[69] Adding to this, early detection of cardiac injury through biomarkers like troponins and natriuretic peptides, and imaging techniques such as echocardiography with strain imaging, is crucial during and after treatment.[63]

Secondary Prevention

For established cardiotoxicity, standard HF therapies are indicated. ACE inhibitors and β-blockers (classical HF therapy) are proven treatments for CTRCD.[70] Whereas statins and aldosterone antagonists remain under investigation (awaiting more trial evidence).[71] In practice, HF therapies (ACEi, β-blockers, statins, aldosterone antagonists) should be initiated when LVEF falls by ≥10% or GLS declines by >15% from baseline.[70] Notably, this recommendation applies even in the absence of elevated biomarkers. However, biomarkers should be interpreted with caution: troponin rises are very sensitive but not highly specific and over-reliance on biomarker elevations may lead to unnecessary interventions.[70]

Multidisciplinary Care

CO is an emerging subspecialty that addresses the CV toxicities in cancer patients. There is a need for equitable CO care across community and academic settings, and there is a suggestion to establish protocols and integrate telehealth to alleviate disparities.[72] Researchers have highlighted the gaps in awareness of instructions and training among healthcare professionals, and they suggest the implementation of national educational initiatives.[73] An integrated model combining CO rehabilitation with traditional cancer rehabilitation was proposed in 2023. The model highlights the importance of early intervention to address CV, physical, and psychological impairments simultaneously.[74] This combined approach could increase long-term survival. Drawing a parallel, researchers also recommend establishing an interdisciplinary CO team that combines artificial intelligence (AI) to generate precision-based risk analysis, early cardiotoxicity detection, and targeted interventions, promoting health equity.[75] Table 4 summarizes the prevention and management strategies.

Table 4: Prevention and management strategies

Strategy	Agents / Actions	Level of evidence / notes	Reference
Primary prevention	Dexrazoxane; SGLT2 inhibitors; imaging/biomarker surveillance	Dexrazoxane FDA-approved; SGLT2 class I in HF; early detection via troponin / BNP / GLS	[63-69]
Secondary prevention	ACE inhibitors; β-blockers; statins; aldosterone antagonists	Initiate if LVEF ↓≥10% or GLS ↓>15% from baseline	[70]
Multidisciplinary care	Integrated cardio-oncology teams; telehealth; rehabilitation programs	Improves equity; early intervention	[72-74]

↓: Indicates decrease, SGLT2: FDA: Food and drug administration, HF: Heart failure, BNP: B-type natriuretic peptide, GLS: Global longitudinal strain, LVEF: Left ventricular ejection fraction

Section 7: Future Directions

However, it is critical that AI models be trained on diverse, representative datasets to prevent algorithmic bias and ensure equitable benefit.[76] Blending AI and genomics into CO can greatly improve the management and avoidance of cardiac toxicity in patients undergoing treatments for cancer. AI has shown great potential in improving risk assessment and clinical decision-making, although there are certain drawbacks when it comes to clinical use and data consistency.[77] In addition, newer studies have highlighted the use of machine learning (ML) algorithms to analyze complex patient data, providing insight into cardiotoxicity mechanisms and treatment strategies.[78] For example, an AI model called AI-CTRCD was developed to predict chemotherapy-related cardiac dysfunction risk from baseline ECGs.[79] ML algorithms trained on standard echocardiographic strain measurements have been used to anticipate early cardiac injury in pediatric cancer survivors.[80] Emerging ML approaches have also identified genetic variants associated with anthracycline cardiotoxicity in childhood cancer survivors, informing integrated risk models.[81] Emerging research encourages a more comprehensive approach to risk assessment, incorporating new biomarkers and genomics into CV evaluation may personalize patient care.[82] In this spirit, emerging approaches (e.g., genomics-driven risk scores) could further refine risk stratification, but these require prospective validation in large studies.[81,83] Protein corona testing, which analyzes the layer of blood proteins that adsorb onto nanoparticles, is an AI-driven, non-invasive biomarker method to detect patterns of proteins linked to cardiotoxicity.[84] This novel approach may enable even earlier detection of cardiac injury and better outcomes. Likewise, studies of multiple blood biomarkers highlight that tracking changes in a panel of markers (not just troponin or BNP), including ultrasensitive troponin I, high-sensitivity CRP, NT-proBNP, growth differentiation factor 15 (GDF-15), myeloperoxidase, placental growth factor, soluble fms-like tyrosine kinase-1, and galectin-3 can improve risk prediction.[76,85] Some recent work emphasizes the genetic underpinnings of anthracycline cardiomyopathy and calls for large-scale genomic cohorts to refine risk classification.[82] Future research should focus on assembling large multiethnic genomic cohorts, conducting prospective AI/ML validation trials, identifying novel biomarkers beyond troponin/BNP, and explicitly designing inclusive datasets to mitigate bias.[76,83]

CONCLUSION

Cancer therapies save lives but impose significant CV risks that compromise long-term survivorship. To mitigate these threats, collaborative efforts must prioritize early detection, personalized prevention, and equitable care.

For clinicians:

- Adopt advanced surveillance: replace routine LVEF with speckle-tracking echocardiography (GLS); a >15% GLS decline signals subclinical dysfunction.
- Stratify risks proactively: consider racial disparities (e.g., 2-3× higher cardiotoxicity in Black/Hispanic patients) and prior CVD history.
- Intervene early: initiate dexrazoxane for high-dose anthracyclines; start ACEi/β-blockers at GLS/LVEF deterioration (not wait for symptoms).

For researchers:

- Resolve biomarker limitations: validate multi-marker panels (troponin + GDF-15/galectin-3) to improve specificity.

Address disparities: investigate socioeconomic/genetic drivers of racial inequities in cardiotoxicity.

- Translate AI tools: Prospectively test ECG- or imaging-based algorithms for real-world risk prediction.

For Policy-Makers:

- Fund integrated CO programs: bridge institutional silos between cardiology, oncology, and rehabilitation services.
- Ensure equitable access: mandate insurance coverage for GLS echocardiography and cardiac MRI across care settings.
- Support survivor longevity: implement lifelong cardiac monitoring for high-risk groups (e.g., pediatric cancer survivors, radiation recipients).

Surviving cancer should not entail enduring preventable heart disease. By embedding CV protection into oncology practice through vigilant monitoring, targeted therapies, and inclusive research we can secure both quantity and quality of life for cancer survivors.

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