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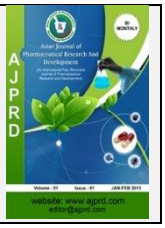

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Review Article

Chemotherapy-Induced Cardiotoxicity: Comprehensive Review of Mechanisms, Diagnosis, and Management

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A B S T R A C T

Background: Chemotherapy-induced cardiotoxicity is a perilous consequence that limits the use of potent anticancer medicines, especially anthracyclines. Notwithstanding progress in oncology, cardiovascular toxicity continues to be a significant contributor to morbidity and mortality among cancer survivors.

Objective: This review examines the molecular mechanisms, diagnostic approaches, and management strategies for chemotherapy-induced cardiotoxicity, emphasizing the need for early detection and interdisciplinary collaboration between cardiologists and oncologists.

Key Findings: Cardiotoxicity manifests as left ventricular dysfunction (LVD), arrhythmias, or heart failure (HF), with anthracyclines and trastuzumab being the most implicated agents. Advanced imaging (e.g., strain echocardiography, cardiac MRI) and biomarkers (troponin, NT-proBNP) enable early detection before irreversible damage occurs. Dexrazoxane, ACE inhibitors, and beta-blockers show promise in prevention and treatment, though optimal protocols remain under investigation.

Conclusion: Proactive monitoring and personalized cardioprotective strategies are essential to balance oncological efficacy with cardiovascular safety. The following studies require concentrating on extensive trials to enhance risk classification and therapy strategies.

Keywords: Anthracyclines, Cardiotoxicity, Chemotherapy, Cardio-Oncology, Heart Failure.

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INTRODUCTION

Chemotherapy and other oncological pharmaceuticals are formulated to treat cancer [1]. As cancer therapy has improved its effectiveness in curing cancer, we have discovered that these life-saving medications can also induce difficulties in the cardiac and vascular systems, referred to as cardiotoxicity[2]. Cardiotoxicity may arise during cancer therapy or manifest within days, months, or years following cancer treatment, even after patients achieve remission.

Chemotherapy-induced carddiotoxicity will diminish the quality of life and elevate the risk of cardiac mortality [3]. Cardiotoxicity is still a very significant topic in clinical practice, with no data focused on clinical trials [4]. Important scientific societies support the publication of this critical clinical guidance. Cardiotoxicity is any kind of damage to the heart that is caused by cancer treatments like chemotherapy, radiation, and the cancer itself [5].

This damage can be functional or structural. While we concentrate on myocardial injury, cardiotoxicity will cause other heart problems, such as pericardial, valvular, or coronary artery disease [6, 7]. Cardiotoxicity is frequently linked to left ventricular dysfunction (LVD). However, this correlation is not universally applicable, and unanimity among oncologists and cardiologists is typically lacking [2].

Chemotherapy works under the general concept of impairing the mitotic and metabolic processes of cancer cells [1]. Unfortunately, chemotherapy affects normal cells and tissues as well, resulting in various moderate to severe side effects such as nausea and vomiting, bone marrow suppression, and cardiovascular side effects such as hypotension, tachycardia, arrhythmias, and cardiac failure. Cardiotoxicity is a term used by the National Cancer Institute to describe toxicity that affects the heart [8]. Certain chemotherapeutic drugs can induce cardiotoxicity, with anthracyclines being particularly associated with more prevalent and frequent adverse effects. These drugs should not be administered to anyone at elevated risk of cardiac complications [9]. Cardiotoxicity is most common in people who have asthma, diabetes, liver disease, or a history of heart disease [10]. After receiving potentially cardiotoxic chemotherapy, a patient can develop heart failure (HF) [11]. The American Heart Association and American College of Cardiology Foundation (AHA/ACCF) categorize cancer patients receiving potentially cardiotoxic treatment as having Stage A heart failure (HF), indicating that these patients are at risk of progressing to more advanced stages (B to D) of HF [12]. People who are getting potentially cardiotoxic chemotherapy are thought to have Stage A HF. However, it is unknown how quickly people with other types of HF move on to more advanced stages, where treatment is usually needed [13].

There is a notable deficiency in research about cardiotoxicity treatment, with clinical practice primarily reliant on restricted studies and patient awareness [14,17]. The European Society for Medical Oncology released Clinical Practice Guidelines for Cardiotoxicity Control in 2012 to aid in cardiotoxicity management. Cardiotoxicity is a serious problem in clinical practice, but there is no data focused on clinical trials [14].With the support of major scientific societies and close cooperation between cardiologists and oncologists, the release of these important clinical recommendations is the first step toward building solid data in cardiotoxicity treatment [2]. Cardiotoxicity is a recognized adverse effect of chemotherapy. Instances of cardiac damage in toddlers exposed to doxorubicin were electrocardiograms (ECGs), changes in blood pressure, arrhythmias, myocarditis, pericarditis, myocardial infarction, and cardiomyopathy. All of these can lead to left ventricular dysfunction (LVD) or congestive heart failure (CHF) [15].

The Cardiovascular Review and Evaluation Committee decides how cardiotoxicity is currently classified for oncologists. This category includes cardiotoxicity linked to trastuzumab and the ESMO Clinical Practice Guidelines [2]. Cancer now affects more than one of every three individuals in their lifetime, and it is the leading cause of death in developing countries, along with cardiovascular disease [16]. Cancer is the second most important cause of mortality in the United States, responsible for one in every four deaths. The examination of these poisons is yielding novel insights for the cardiology community regarding cardiomyocytes and their life cycle [13]. This plan relies on three methods to describe and monitor cardiovascular diseases: alterations in the myocardium's contractility, issues with blood flow to the arteries, and issues with the heart's electrical system [5]. Anti-vascular effects or target or immunological agents are not looked at in this study. They are only mentioned to show how they are similar to and different from chemotherapy, as shown in Figure 1 [18].

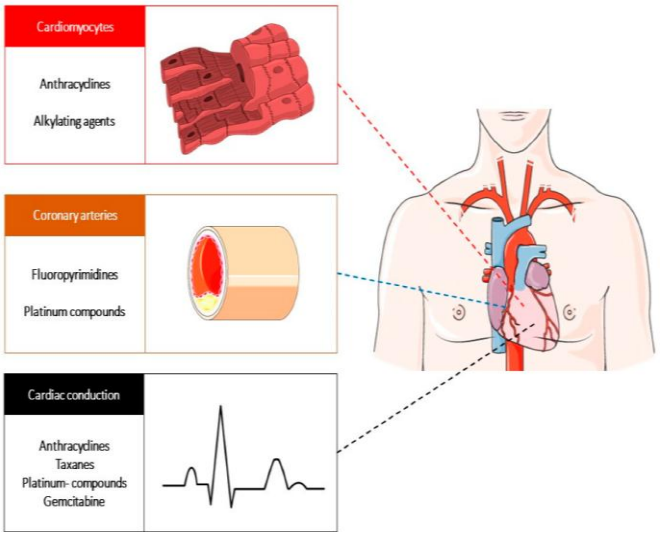

Figure 1: The spectrum of cardiac toxicity and the most common related causative antineoplastic agents [18].

Cancer disease

Cancer is an abnormal disease that divides and invades nearby tissues without control. The blood and lymph systems of cancer cells will spread to other areas of the body as well. Several major cancer forms exist [19]. Cancer of the skin or tissues thatline or encapsulate internal organs is carcinoma. Carcinoma Sarcoma is a cancer that begins in the blood or other connective or supporting tissue, including bones, cartilage, fat, muscles, or blood vessels. Leukemia is cancer that starts in blood-forming tissue, including the bone marrow, and leads to excessive irregular blood cells. Cells that begin in cells of the immune system are lymphoma and multiple myeloma. Cancers of the central nervous system begin in the tissues of the brain and spinal cord. Malignancy is another term for cancer. Cancer cells do not behave like normal cells; they develop into tumors and can spread to other parts of the body [12]. A study done before the current HF care and LVEF screening during chemotherapy found that 2.2% of over 4,000 patients receiving anthracyclines had clinical HF and 71% of those patients died because of it [11].More recently, Cardinaleand his colleagues looked at patients who took more than 500 mg/m² of anthracyclines [9]. They found LV dysfunction in 63% of those who were followed up for 10 years but only 18% of those who took less than 500 mg/m².Even with modern heart failure care, a study from 2010 found that LV activity did not change much in 45% of patients with anthracycline-induced heart failure [9]. Contrary to popular belief, cardiotoxicity caused by trastuzumab can be reversible if the medication is stopped

and HF therapy is undertaken [5]. As a result, cardiotoxicity can be described based on the underlying pathways and reversibility. This method can predict irreversible HF and keep track of the right treatment, as shown in Table 1.[8].

Table 1: Comparing the performance of Type I and Type II Cardiotoxicity[8].

Feature	Type I (Anthracycline-like)	Type II (Trastuzumab-like)
Cellular Mechanism	Cell death	Cell dysfunction
Dose Related	Cumulative	Non-cumulative
Reversibility	Permanent	Reversible

Cancer treatment

Numerous modalities exist for cancer treatment. The treatment received is contingent upon the specific form of cancer and its severity. All cancer patients will get a singular treatment.Nevertheless; many patients undergo a combination of treatments, including surgery, chemotherapy, and radiation therapy [19]. Surgery, used to cure cancer, is a technique in which a surgeon removes cancer from the body. Radiation therapy is a cancer treatment modality that uses high doses of radiation to eradicate cancer cells and reduce tumor size [19].

Chemotherapy is a method of cancer treatment that employs the use of drugs to kill cancer cells. Immunotherapy is a cancer treatment modality that utilizes the immune system to combat cancer [4,5]. Targeted therapy is a cancer treatment that addresses the changes in cancer cells that cause them to develop, differentiate, and spread. Discover how targeted treatment functions against cancer and the most frequent side effects that can occur [5]. Hormone therapy slows or stops the growth of breast and prostate cancers that depend on hormones to grow. Stem cell transplants bring back blood-forming stem cells in cancer patients whose stem cells were killed by very high doses of chemotherapy or radiation therapy. Precision medicine helps doctors choose treatments that are more likely to help patients based on several factors [6]. The radiation can hurt the heart, even if it is only slightly. Such damage can lead to heart problems like constrictive pericarditis, pericardial effusion, coronary artery disease, restrictive cardiomyopathy, and heart valve problems [6]. Patients undergoing radiation therapy for breast, lung, esophageal, or mediastinal cancer can receive radiation to the heart [14].

Cardiotoxicity has been observed in 2-4% of patients with the antimetabolite 5-fluorouracil or its equivalents. 5-fluorouracil may induce coronary vasospasm, potentially resulting in chest discomfort, myocardial ischemia, infarction, and mortality [20]. These side effects are more likely to occur in people who have pre-existing or previously undocumented CAD, have had prior radiation therapy, or are taking cisplatin, which can predispose to ischemia on its own. When the 5-fluorouracil is stopped, these side effects go away [4]. Capecitabine, a prodrug converted in the body to 5-FU, exhibits comparable cardiotoxic effects. In patients with confirmed coronary artery disease and ischemia who have not had revascularization, the use of 5-fluorouracil and its equivalents should be avoided [20]. Before starting 5-fluorouracil treatment, elderly patients or those with several CAD risk factors should have myocardial perfusion imaging [21]. About 25 TKIs are either in commercial use or are conducting advanced clinical trials [5]. Taxanes, such as paclitaxel and docetaxel, are used to treat cancers of the breast, lung, and ovary. These substances can cause ischemia, arrhythmias, and CHF. Myocardial ischemia has been identified in up to 5% of patients receiving docetaxel [8].

Cardiotoxic effects of chemotherapeutic agents

Cardiotoxicity (CT) is a broad word that refers to "toxicity that affects the heart." This word describes the direct effect that chemotherapy has on the heart and blood vessels, as well as the unintended effect that occurs because of thrombogenicity or a change in blood flow [22]. The presence of cardiotoxic diseases, even when asymptomatic, adversely impacts the patient's cardiac prognosis and significantly restricts treatment options [5,23]. Researchers have tried to figure out how cardiotoxicity works so that they can better watch cancer patients who have heart problems [16]. This is because heart damage can make cancer treatments less effective and cause permanent changes to the myocardium. This is because heart damage can reduce the effectiveness of cancer treatments and result in permanent changes to the myocardium. Ensuring cardiac function remains an ongoing challenge for the pharmaceutical business and the physicians managing these side effects. It should be easier to figure out which patients are at risk, come up with ways to keep that from happening, and quickly treat cardiotoxicity when it does happen so that management works better [14, 22].

Data are scarce on the cause of the emergence of heart dysfunction during chemotherapy and the vulnerability of patients to develop cardiotoxicity [24]. Some results show that patients who don't have a history of heart failure may develop heart failure symptoms as a direct result of the combined dosage they received. This has led to lower chemotherapy doses being used, which makes them less effective [25]. Acute or subacute cardiotoxicity can occur at any time during therapy. This condition can be shown by a number of different types of arrhythmias, issues with ventricular repolarization and QT cycles, acute coronary syndromes or pericardial response, and changes in myocardial activity [8]. Cancer treatment primarily consists of chemotherapy, radiation, and surgery; both chemotherapy and radiation considerably contribute to cardiotoxicity. Not all cancer patients experience cardiotoxicity; numerous factors influence the cardiotoxicity generated by cancer therapies [26]. This scenario is illustrated in Figure 2.

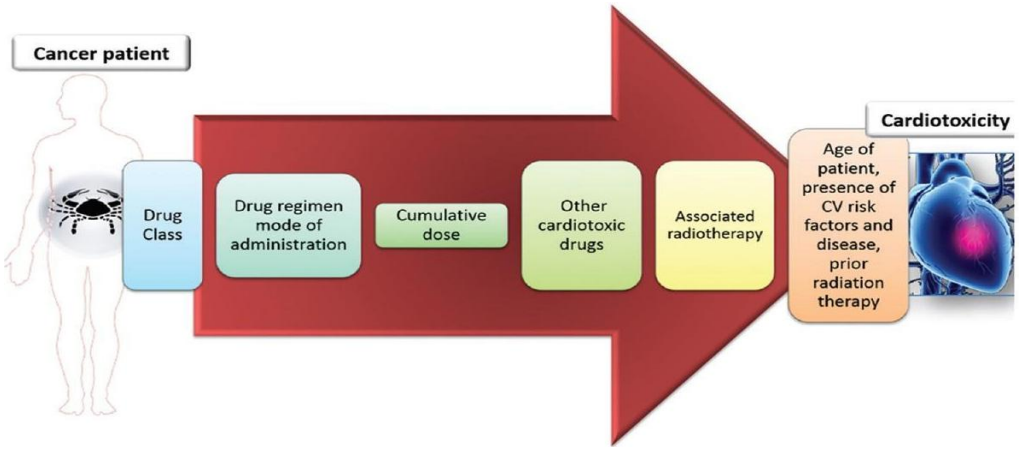

Figure 2: Risk factors attributed to the diverse course of chemotherapy-induced cardiotoxicity [26].

Doxorubicin-induced cardiotoxicity

Anthracyclines like doxorubicin (DOX), daunorubicin, epirubicin, and idarubicin are very good at fighting acute lymphoblastic and myeloblasticleukemias [16]. DOX has been found to cover a lot more types of cancer, such as solid tumors like breast cancer, sarcomas, and pediatric solid tumors like Wilms' tumor, as well as hematological cancers like Hodgkin's disease, non-Hodgkin lymphomas, and leukemias. Hodgkin's cardiotoxicity induced by anthracyclines can manifest as either acute or chronic [9, 14]. Cardiotoxicity induced by anthracyclines can manifest as either acute or chronic. Acute cardiotoxicity, including pericarditis, myocarditis, orarrhythmias, is generally reversible and manageable during treatment. In contrast, chronic cardiotoxicity, which may manifest decades post-treatment, is severe and clinically significant, substantially impacting overall morbidity and mortality and requiring long-term management [11].This study is mostly about DOX-induced cardiotoxicity [10].

Currently, there are no definitive guidelines for managing chemotherapy-induced cardiotoxicity; nevertheless, some small evidence suggests that neurohormonal antagonists may be beneficial in treating and preventing this condition [27]. Multi-center trials are needed to develop guidelines for chemotherapy-induced cardiotoxicity. Furthermore, close cooperation between the cardiologist and oncologist is highly advised to develop a clear treatment plan for the patients [4]. Along with lowering the total amount of anthracycline given, other steps can be taken to lower the risk of cardiac cell apoptosis.It is possible to reduce cardiac toxicity even more by giving anthracyclines as infusions instead of boluses and by encapsulating doxorubicin in liposomes [11]. In combination with doxorubicin or epirubicin, dexrazoxane, an EDTA-like chelator, can reduce the risk of cardiotoxicity. This is restricted to patients who have received a combined dose of doxorubicin greater than 300 mg/m² [8].Table2 provides information related to the cardiovascular effects of common chemotherapy agents.

Table 2: Cardiovascular Effects of Common Chemotherapy Agents [8].

Drug	Class & Mechanism	Myocardial Effect	Cardiovascular Toxicity
Anthracyclines	Polyketides; multiple anticancer mechanisms.	Reversible/irreversible; long-term common.	CHF.
Trastuzumab	Monoclonal antibody inhibits HER2/neu receptor.	Reversible/irreversible; long-term rare.	CHF, hypertension.
Imatinib	Tyrosine kinase inhibitors target Bcr-Abl, c-kit, and PDGFR.	The condition is reversible and not long-term.	CHF, LVEF depression.
Cyclophosphamide	Alkylating agents inhibit DNA replication.	Irreversible; no long-term.	CHF, hemorrhagic myocarditis (high doses).
Cisplatin	Platinum-based inhibits DNA metabolism.	Irreversible (if infarction).	Ischemia, venous thrombosis, hypertension.
Fluorouracil	Pyrimidine analog.	Irreversible (if infarction).	Ischemia, MI.
Paclitaxel	Anti-microtubule agents target tubulin.	Reversible; no long-term.	CHF, bradyarrhythmia.
Vinblastine	Vinca alkaloid inhibits microtubule formation.	Reversible; no long-term.	Raynaud's phenomenon.

A critical part of figuring out how cardiotoxicDOX is how much of it is given over time. It cannot be more than 500 mg/m², or the risk of congestive heart failure (CHF) will go up rapidly. The likelihood of having CHF increases from 4% at a cumulative dose of 500–550 mg/m² to 18% or 36% at cumulative doses of 551–600 mg/m² or above 600 mg/m², respectively [11]. As compared to the approximate values of their siblings, 30-year childhood cancer survivors have a 15-fold higher risk of heart failure and a 10-fold higher rate of other cardiovascular disorders, according to a retrospective analysis[29]. Heart rhythm problems that do not cause any symptoms, high blood flow, thickening of the pericardium, heart dilation, and cardiomyopathy are all signs of a problem with the heart [5]. Under a microscope, patches of patchy and

interstitial fibrosis with sparse vacuolated cardiomyocytes can be seen [29].

Some myofibrils are also lost, and vacuoles break down. This process leaves the remaining peripheral Z disks without filaments and much membrane-bound space.Researchers found chromatin disorganization in the nucleus, where pale staining fibers and filaments partially substituted the chromatin [16]. The maximum cumulative doses of anthracyclines vary depending on the specific drug, with doxorubicin having a recommended limit of 400–450 mg/m², epirubicin up to 900 mg/m², daunorubicin up to 800 mg/m², and idarubicin up to 160 mg/m². Surpassing these thresholds markedly elevates the risk of cardiotoxicity, including congestive heart failure (CHF) and irreversible myocardial injury. Meticulous monitoring and compliance with these cumulative dose limitations are crucial for reducing long-term cardiac problems in patients receiving chemotherapy [14].

Although the findings are positive, further research is needed to explore all facets of this therapeutic approach [27].The Finland Herceptin study found that a nine-week treatment plan using trastuzumab along with docetaxel and vinorelbine was linked to lower heart damage while still being effective against cancer.The peak serum concentration achieved during administration is another important factor in chemotherapy-induced cardiotoxicity. However, in a major meta-analysis conducted by Van Dalen, patients receiving doxorubicin with peak doses of less than mg/m² were compared to those receiving higher doses of up to mg/m² [28]. There was no significant difference between the two groups in terms of clinically manifested heart failure or overall patient survival. A randomized clinical study of 1086 breast cancer patients receiving epirubicin found the same thing. The drug was given in two different serum peakdoses, which are 83 mg/m³ and 110 mg/m³ [4].

DOX is incredibly hazardous to the heart because of its remarkable impact on mitochondria. The heart, as a pump that circulates blood across the body, needs much energy and, hence, has a lot of energy-producing mitochondria [28].Most of the reactive oxygen species (ROS) are found in mitochondria. This is because electrons escape from the electron transport chain and are absorbed by oxygen there, which is where superoxide is made [16]. Many chemotherapy drugs cause rapid cell death or necrosis, stop cancer cells from multiplying and blood vessel growth, or lower their ability to heal. Figure 3 illustrates these effects on both multiplying cancer cells and the heart.Trastuzumab is either directly harmful to the heart or makes the harmful effects of anthracyclines worse by affecting ErbB2 receptors, which are found in the myocardium and help keep the heart healthy [4]. Anthracyclines are a type of chemotherapy that is widely used. They cause damage to mitochondria, changes in ATP synthesis, and cell death, as well as more free radicals that affect the cell membrane [8].

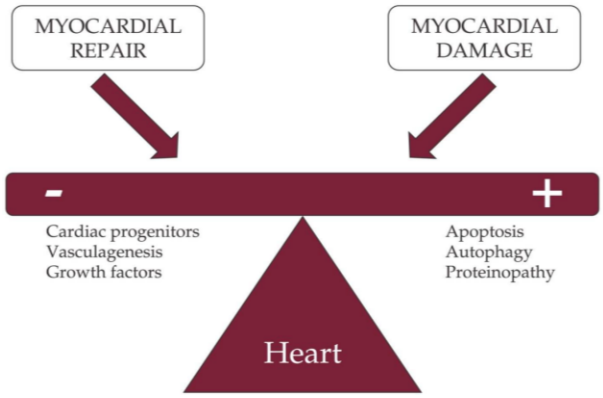

Figure 3: The direct impact of chemotherapeutic agents on the myocardium results in cardiotoxicity [8].

Diagnosis of Cardiotoxicity

Cardiotoxicity is a growing concern associated with the use of chemotherapy and radiotherapy to treat neoplastic diseases. Early detection during follow-up is critical, and diligent monitoring is advised [4]. Echocardiography and nuclear medicine are common ways to check left ventricular ejection fraction in clinical settings, but they are not excellent at finding early heart damage [30]. Clinicians also have access to new tools such as speckle-tracking screening, cardiac magnetic resonance, and cardiac circulating biomarkers [30]. Table 3 shows the techniques that are used in cardiac function assessment. While patients with cardiotoxicity are sometimes asymptomatic, and the diagnosis is made on a regular echo, classic symptoms and signs of HF can occur and should be explored regularly in all cancer patients for an early diagnosis [31]. However, clinical diagnosis can be complicated because cancer patients often experience fatigue, asthenia, fragility, or even dyspnea for non-cardiologic causes.

The NYHA functional class (I–IV) and the AHA/ACC classification are suggested ways to find out the clinical status (A–D) of people with HF [3]. As for other causes of HF, a fully normal ECG usually indicates normal LVEF, so an ECG should be performed before and regularly during therapy. Arrhythmias, QT prolongation, bundle branch block, ischemia, or resting tachycardia are all examples of ECG abnormalities in cardiotoxicity patients [30].

Nuclear cardiac imaging and cardiac magnetic resonance (CMR) are also excellent methods for evaluating cardiac activity. Researchersdeveloped that CMR is a fantastic way

to find out what causes LVD, right ventricular dysfunction, and myocardial fibrosis with late gadolinium enhancement [32]. CMR may also be used to classify anatomical defects in type 1 cardiotoxicity. These techniques can perform as well as an echo in the follow-up, but their scarcity is their main drawback [16].

Table 3: Echocardiography Techniques for Cardiac Function Assessment[23].

Technique	Procedure/Findings	Sensitivity	Remarks
2D Echocardiography	Preferred for cardiac imaging.	Good sensitivity, noninvasive, cost-effective. Limited for subtle myocardial changes.	Widely available and has no radiation. Limited by poor acoustic windows.
Myocardial Strain Imaging	Detects peak systolic longitudinal strain early.	Predicts cardiomyopathy.	Interobserver variability requires high image quality.
Speckle Tracking Imaging	Assesses myocardial deformation.	Predicts cardiomyopathy.	Vendor-dependent scales require high image quality.
3D Echocardiography	Operator-independent LVEF measurement. >10% decrease below LLN suggests cardiotoxicity.	Reproducible LVEF measurement.	Interobserver variability, technically demanding.
Stress Echocardiography	Assesses inducible ischemia and myocardial viability.	Not explicitly reported.	Useful for ischemia and viability assessment.
GLS	>15% reduction from baseline suggests cardiotoxicity risk.	Early detection of cardiotoxicity.	Sensitive for cardiotoxicity in patients on cardiotoxic therapies.
Troponin I, T	It can identify damage to cardiomyocytes and may be valuable in detecting acute cardiotoxicity.	Clinical and prognostic relevance is significant; high-sensitivity assays demonstrate considerable sensitivity, thereby enhancing the negative predictive value.	There is inadequate evidence to determine the importance of minor increases. Variations among various assays

Cardiac biomarkers

Natriuretic peptides are the predominant cardiac biomarkers utilized in heart failure and cardiotoxicity.There is no evidence that NT-proBNP can be utilized to manage cancer treatment decisions, including the initiation or cessation of chemotherapy [32]. Dexrazoxane, a cyclic form of eidetic acid, is a heart-protecting drug that works well against heart damage caused by anthracyclines [14].The Spanish Congress of Cardiology had a short report on 50 patients with LVD who had been through chemotherapy and were treated with special heart drugs that was shownin 2015. The report indicated that 62 percent of these patients had their ejection fractions healed in an average of 14months [9].

The SOLVD study found that only enalapril was better than the other drugs at slowing down or fixing left ventricular dilatation in patients who did not have any symptoms [9]]. This assumption was stated in the ESC position paper on cancer therapies and cardiovascular toxicity, even though there was not much evidence. The cardio-oncology team needs to carefully look at the prognostic effects of changing, minimizing, or stopping cancer treatment and think about how LVD might affect the outcome [27]. In this case, the decision must be made not only on oncological criteria (prognosis, options, dosage, timetable of chemotherapy, etc.) but also on cardiological criteria (HF status, cardiovascular risk factors, LVEF, cardiovascular drugs, etc.). Finally, the administration of patients with regenerated ejection fraction is deficient in facts [12].

The prognosis for patients with cardiotoxicity relies on cancer death, LVD and HF incidence, and clinical conditions. HF is malignant, with 50% dying in the next five years, while cancer survival estimates depend on individual cancer [5]. The condition is known to be a malignant disease. When making a cardiotoxic decision to stop chemotherapy, one must consider the entire prognostic condition and available options [3].As previously stated, patients with restored ejection fraction have a greater prognosis than those with HF and decreased or retained ejection fractions. Still, other considerations, such as cancer healing and the need for additional cancer or cardiovascular therapies during the follow-up, should be considered [13].

Prevention of Cardiotoxicity

First and foremost, cardiotoxicity reduction begins with an accurate evaluation of cardiovascular vulnerability and predisposing factors, as shown in Table 5. We lack specific metrics to evaluate global cardiovascular risk, including previous cancer or chemotherapy (notably anthracyclines). However, they may be regarded as risk factors for cardiotoxicity and cardiovascular disease [24]. As a result, patients with several risk factors, especially inadequate control and a history of cardiovascular disease, should be treated in the same manner as high-risk patients [2]. Cardiotoxicity restricts the effective application of antineoplastic therapies. Cardiotoxicity can be minimized or prevented through various measures.To lower the risk of cardiotoxicity caused by anthracyclines, a complete plan should be used. This plan should start with steps taken before chemotherapy, like finding out what risks the patient faces and not giving anthracyclines to people who are at high risk when they can [26].

Table 5: Precursor and associated risk factors for cardiovascular disease and cardiotoxicity [2].

Current Status	Risk Factors or Precursor factors
Current myocardial disease	Previous heart failure and/or LVD Any cardiomyopathy (i.e., hypertrophic) or significant cardiopathy (i.e., hypertensive) Coronary artery disease Significant arrhythmias
Previous cardiotoxic cancer treatment	Previous anthracycline use Previous thoracic radiotherapy
Cardiovascular and lifestyle risk factors	Smoking, arterial hypertension, obesity, etc.

Second, it is critical to evaluate basal heart function before beginning therapy, taking into account more than just left ventricular ejection fraction (LVEF). If any important findings are made about the structure or function of the heart at rest, like LVEF being below the lower limit of normal values, the chance of cardiotoxicity is thought to go up [14]. The function of cardiac biomarkers is more debatable. It is uncertain if patients with elevated basal cardiac biomarkers (NT-proBNP and troponin) are at a greater risk of cardiotoxicity despite having a worse prognosis [16]. Only one trial found that cardioprotective therapy is effective in patients undergoing anthracyclines as troponin levels rise during treatment. The most daunting part of professional practice is determining what to do if any of these determinations/decisions are uncommon. In these cases, cardio-oncology procedures must be followed to assess the frequency of repeating the scans at follow-up and the treatment of these anomalies [27]. Tomescu et al. discussed a small study of 60 breast cancer patients who were given anthracyclines for six months. The study indicated that nebivololmight help people avoid LVD more than a placebo [27].

Patients undergoing chemotherapy who exhibit signs of impaired cardiac function meet the international criteria for heart failure. Early recognition and intervention are crucial, as managing heart failure in cancer patients can significantly impact prognosis. A multidisciplinary approach is essential for optimizing treatment strategies. Amide, cisplatin, ifosfamide, and taxane shave been associated with cardiac dysfunction [33]. If direct cardiotoxicity is thought to be happening, treatment methods for anthracycline-induced cardiotoxicity should be used. Furthermore, as shown in Figure 4, a multidisciplinary assessment should be done to rule out other possible heart problems.

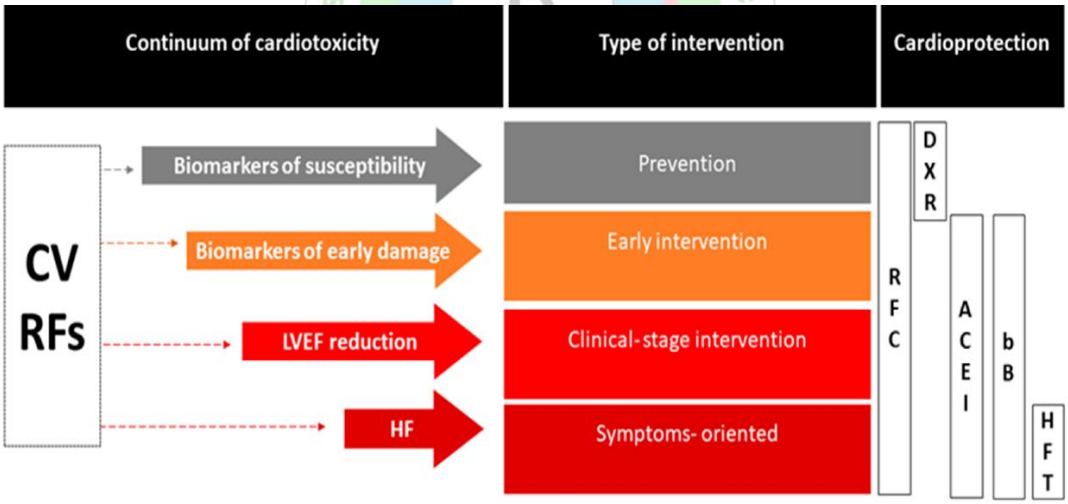

Figure 4: A summary of how cardioprotective drugs are used in clinical practice today, grouped by the level of cardiotoxicity [23].

Chemotherapy-induced cardiotoxicity remains a significant clinical challenge, particularly with anthracyclines, which are among the most widely used and effective chemotherapeutic agents. Shaikh and Shih highlight that anthracyclines are the most implicated class of drugs in causing cardiotoxicity, emphasizing the importance of using the lowest effective dose to minimize risks [34]. They advocate for close surveillance for left ventricular dysfunction (LVD) during and after treatment, as cardiotoxicity can manifest years later, leading to heart failure (HF). Even with these precautions, the authors say that there are still no risk prediction models that can find the patients who are most likely to experience cardiotoxicity. This shows how important it is to have long-term monitoring and better risk stratification tools [34,35].

Advances in non-invasive cardiac imaging have significantly improved the ability to detect cardiotoxicity at earlier stages [34]. Modern imaging methods, like echocardiography and strain imaging, can find small problems in the contractile function of the myocardium before they show up in the global systolic function of the left ventricle (LV) [8].

These advancements enable clinicians to intervene earlier, potentially preventing irreversible cardiac damage [8, 34]. Researchers suggest that people who go from Stage A to Stage B heart failure or stay in Stage A three months after

starting potentially cardiotoxic chemotherapy are more likely to have changes in their heart failure status that last for 6 to 24 months [13].This study indicates that early monitoring of heart failure stages may act as a prognostic indicator for long-term cardiac prognosis in cancer patients [13,35,36].

In addition to myocardial dysfunction, chemotherapy agents can also induce electrophysiological abnormalities. Cancer treatment drugs, particularly those known to cause QT prolongation, can lead to life-threatening arrhythmias [21]. With the increasing survival rates of cancer patients, the researchers stress the importance of closely monitoring ECG changes and arrhythmias in this population to prevent fatal cardiac events [21,37]. Studied shows how important it is to look at both changes in LV volumes and changes in LV strain because together, they give a fuller picture of how the heart works after chemotherapy [21]. This approach can help clinicians better interpret the severity and progression of cardiotoxicity [37,38].

Finally, the dual-edged nature of chemotherapeutic agents, such as doxorubicin, which are highly effective against cancer but pose significant risks of cardiotoxicity at higher doses [10]. The writers stress that these drugs' clinical benefits are often limited by their negative effects on the heart [39].

This means that doses need to be carefully managed, and strategies need to be created to protect the heart [40-43].Together, these studies indicate that cardiotoxicity caused by chemotherapy is complicated. Stresses the need for early detection, close monitoring, and personalized treatment plans to lower risks and improve outcomes for cancer patients.

CONCLUSION

The use of anthracyclines and trastuzumab in cancer treatment leads to significant heart problems, including heart failure and arrhythmias, because of chemotherapy-induced cardiotoxicity. The identification of heart damage requires advanced imaging and cardiac biomarkers for early detection before heart damage becomes permanent. The combination of cardioprotective drugs such as dexrazoxane with ACE inhibitors and beta-blockers, together with regular monitoring, serves as preventive measures to decrease the risk.

The management of heart complications needs collaboration between oncologists and cardiologists who create personalized treatment plans according to patient-specific risk profiles. Ongoing research and expanded clinical trials are crucial to optimize treatment procedures, guaranteeing both effective cancer therapy and cardiovascular safety.

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