CARDIOVASCULAR COMPLICATIONS OF CHEMOTHERAPY IN BREAST CANCER: A SCOPING REVIEW

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ABSTRACT

Background: **Chemotherapy remains a cornerstone in breast cancer management but is associated with significant cardiovascular toxicity, which may adversely affect long-term outcomes. Anthracyclines are particularly implicated due to their dose-dependent cardiotoxic effects.**

Objective: **To synthesize current evidence on chemotherapy-induced cardiotoxicity in breast cancer, with emphasis on anthracycline-related cardiac dysfunction, including epidemiology, mechanisms, risk factors, detection, and prevention.**

Methods: **A scoping review of peer-reviewed literature was conducted using PubMed, Scopus, Web of Science, and Google Scholar. Studies evaluating cardiovascular complications of chemotherapy in breast cancer were included.**

Results: **Cardiotoxicity risk is associated with cumulative anthracycline dose, concurrent use of cardiotoxic agents such as trastuzumab, and pre-existing cardiovascular disease. Mechanisms include oxidative stress, mitochondrial dysfunction, and topoisomerase II inhibition. Early detection using speckle-tracking echocardiography and biomarkers such as troponins and natriuretic peptides allows identification of subclinical myocardial injury. Preventive strategies—including dose modification, liposomal anthracyclines, and cardioprotective agents such as dexrazoxane, beta-blockers, and ACE inhibitors—demonstrate benefit.5/13/2026**

Conclusion: **Chemotherapy-induced cardiotoxicity remains a major clinical challenge. Early detection, risk stratification, and integrated cardio-oncology care are essential to improving outcomes in breast cancer patients.**

Keywords: Breast cancer; Anthracyclines; Cardiotoxicity; Chemotherapy; Cardio-oncology.

INTRODUCTION

Breast cancer is the most commonly diagnosed malignancy worldwide and the fifth leading cause of cancer mortality constituting about 6.9% of the total cancer death.[1] It is the leading cause of cancer related death among women in West Africa.[2] Among female globally, breast cancer was the leading cause of cancer-related DALYs, deaths, and YLLs in 2019.[3]

Advances in multimodal therapy including surgery, radiotherapy, chemotherapy, endocrine therapy, and targeted biological agents—have significantly improved survival outcomes.[4] However, these gains have been accompanied by an increasing recognition of treatment-related toxicities, particularly cardiovascular complications.[5] Chemotherapy plays a central role in breast cancer management across disease stages. Commonly used agents include anthracyclines, taxanes, alkylating agents, and targeted therapies such as trastuzumab. While effective, these therapies are associated with systemic adverse effects, among which cardiotoxicity is one of the most clinically significant due to its potential to cause irreversible myocardial injury, heart failure, and increased long-term morbidity and mortality.[6]

Cancer therapy–related cardiac dysfunction (CTRCD) encompasses a spectrum ranging from asymptomatic subclinical myocardial injury to overt heart failure.[7,8] With improved survival and treatment of breast cancer, cardiovascular events in long-term survivors is now on the increase with higher frequencies of cardiotoxicity in patients receiving other medications (e.g. docetaxel and trastuzumab) in addition to anthracyclines, and by patient-related factors including pre-existing cardiovascular disease.[9-11]

With improving cancer survival, long-term cardiovascular health has become a critical component of survivorship care. Early detection of cardiotoxicity using advanced imaging modalities such as speckle-tracking echocardiography and cardiac biomarkers offers an opportunity for timely intervention.[7,12,13]

Early detection of subclinical myocardial changes after chemotherapy encourages prompt initiation of preventive as well as treatment strategies. This can be instituted with established cardioprotective medications such as beta-blockers, angiotensin-converting enzyme inhibitors, or dexrazoxane.[12] Reduction of cardiac events as well as recovery in LV dysfunction associated with cancer treatment can be achieved when LV dysfunction is detected early and cardioprotective therapy is promptly initiated.[14]

Aim of the study: This scoping review aims to synthesize current evidence on chemotherapy-induced cardiotoxicity in breast cancer, with emphasis on anthracycline-related cardiac dysfunction, including mechanisms, risk factors, early detection, and preventive strategies.

METHODS

A scoping review of the literature was conducted to identify and synthesize evidence on chemotherapy-induced cardiotoxicity in breast cancer. A comprehensive search of electronic databases, including PubMed, Scopus, Web of Science, and Google Scholar, was performed for studies published up to 2024. Search terms included combinations of "breast cancer," "chemotherapy," "cardiotoxicity," "anthracyclines," "trastuzumab," and "cardio-oncology." Eligible studies included original research articles, clinical trials, and systematic reviews addressing epidemiology, mechanisms, risk factors, detection, and management of chemotherapy-related cardiac dysfunction. Non-English publications and studies not directly related to cardiovascular complications of breast cancer therapy were excluded. Reference lists of selected articles were also screened for additional relevant studies.

Treatment modalities of breast cancer

The main conventional modalities of treatment for breast cancer are surgery, radiation therapy, chemotherapy, hormone (endocrine) therapy, and targeted therapy (using biologic agents).[15]

Neoadjuvant chemotherapy is advocated in patients with locally advanced breast cancer, including large primary tumors, inflammatory breast cancer, skin or chest wall involvement, and clinically significant axillary nodal disease.[16] These factors are used to determine the treatments to be considered and the sequencing of the therapies in breast cancer management.[17] Surgery is done first in patients who present with early-stage breast cancer (ductal carcinoma in situ and small tumors that are clinically lymph node negative) or with inflammatory breast cancer, while neoadjuvant chemotherapy is advocated in patients with large tumors, skin involvement, or bulky nodal disease.[17]

Radiation therapy generally is done after chemotherapy and surgery while hormone therapy alone can be used in older or frail patients.[17] Biological therapy (targeted therapy) can be used at every stage of breast cancer therapy, before surgery as neoadjuvant therapy or after surgery as adjuvant therapy in HER2-positive patients.[18]

Cancer therapy-related cardiac dysfunction (Ctrcd)

Cancer therapy-related cardiac dysfunction (CTRCD) refers to a spectrum of cardiovascular abnormalities resulting from cancer therapies, characterized by reductions in left ventricular ejection fraction (LVEF), abnormalities in myocardial strain, elevations in cardiac biomarkers, and/or development of symptomatic heart failure following exposure to cardiotoxic cancer treatment.[19]

Various cancer therapies, including chemotherapy, targeted agents, immune therapies, and radiation therapy can result in cardiotoxicity.[20,21] Common adverse cardiovascular events during contemporary cancer therapy can be categorized into five: (i) cardiac dysfunction: cardiomyopathy/heart failure (HF), (ii) myocarditis, pericarditis and pericardial effusion (iii) vascular toxicity, (iv) hypertension, and (v) arrhythmias and QTc prolongation.[20]

In the past, there were several terminologies and definitions describing the spectrum of cancer therapy-related cardiovascular toxicity, which led to inconsistencies in diagnosis and management of the disease.[22] In 2022 however, international definitions were proposed to harmonize these variations.[20] The descriptive term cancer therapy-related cardiac dysfunction (CTRCD) was therefore recommended as it captures the broad spectrum of possible presentations and aetiology of various cancer therapies.[7] The European Society of Cardiology (ESC) guidelines on cardio-oncology in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS) further defined CTRCD based on symptoms, ejection fraction, changes in LV strain, and cardiac biomarkers.[7] (Table 1)

Table 1. Definitions for cancer treatment related cardiac dysfunction (CTRCD).

	Mild	Moderate	Severe	Very Severe
Asymptomatic CTRCD (with or without additional biomarkers, LVEF values are based on 2D echocardiography)	LVEF ≥50% AND new relative decline in GLS by >15% from baseline AND/OR new rise in cardiac biomarkers	New LVEF reduction to a LVEF of 40-49% AND new relative decline in GLS by >15% from baseline AND/OR new rise in cardiac biomarkers	New LVEF reduction to <40%	
Symptomatic CTRCD (with LVEF and supportive diagnostic biomarkers)	Mild HF symptoms, no intensification of therapy required	Need for Outpatient intensification of diuretic and HF therapy	HF Hospitalization	Requiring inotropic support, mechanical circulatory support or consideration for transplantation

Adapted from ESC guidelines on cardio-oncology (2022).[7]

The classification of CTRCD was first reported in 1998 after the introduction of trastuzumab, a monoclonal antibody, for the treatment of breast cancer. It was classified into Type 1 (anthracycline-related, irreversible and dose dependent)[23] and Type 2 (trastuzumab-related, reversible and dose independent).[24] However, with the advent of newer treatments, an updated classification has been proposed in 2019 to further incorporate mechanisms not previously categorized.[25]

- Type 1: Irreversible myocardial damage, dose dependent (i.e., anthracyclines)
- Type 2: Reversible myocardial damage, dose independent (i.e., trastuzumab)
- Type 3: Coronary disease related such as radiation exposure and spasm (i.e., radiation therapy and fluorouracil)
- Type 4: Miscellaneous related to myocarditis or takotsubo cardiomyopathy (i.e., fluorouracil and tyrosine kinase inhibitors)
- Type 5: Indirect which are secondary to conduction abnormalities, arrhythmias, and hypertension (i.e., ibrutinib, fluorouracil, and platinum-based therapy)

Chemotherapy agents affect the heart either directly or indirectly, some commonly used chemotherapeutics in the treatment of breast cancers and their cardiovascular adverse effects are shown in Table 2.[26] In recent times, there is a growing interest in the bidirectional relationship between cancer and heart failure looking beyond the already established effects of cancer therapies.[27] Evidences have shown that cancer in itself might promote heart failure development and heart failure could act as a pro-oncogenic condition.[28]

Table 2. Commonly used chemotherapeutics in the treatment of breast cancer and their cardiovascular effects

Class of drugs	Examples	Cardiovascular side effects
Anthracyclines	Epirubicin, doxorubicin, daunorubicin, idarubicin	Ventricular fibrillation, myocarditis, heart failure, ventricular tachycardia, left ventricular dysfunction, pericarditis, atrial fibrillation
Taxanes	Paclitaxel	Ventricular ectopy, bradycardia, heart block
Alkylating agents	Cyclophosphamide, cisplatin, mitomycin, ifosfamide	Heart block, supraventricular tachycardia, left ventricular dysfunction, bradycardia, atrial fibrillation, arterial thrombosis, myocarditis, pericarditis
Endocrine therapy	Anastrozole, letrozole, tamoxifen	Thromboembolism, valvular dysfunction, venous thrombosis, heart failure, pericarditis, peripheral atherosclerosis, dysrhythmia
Cyclin-dependent kinase inhibitors	Ribociclib, palbociclib, lapatinib, safenib	QTc prolongation
Antimetabolites	Capecitabine, 5-fluorouracil, cytarabine, methotrexate	Congestive heart failure, ventricular tachycardia, coronary artery spasm, ventricular fibrillation, coronary thrombosis, atrial fibrillation
HER-2–directed therapies, Radiation therapy	Pertuzumab, trastuzumab	Heart failure, left ventricular dysfunction, Cardiomyopathy, coronary artery disease, valvular disease pericardial disease, arrhythmias

HER-2 (human epidermal growth factor receptor 2). Adapted from Albini A et.al.[26]

A significant increase in cardiovascular peptides (e.g. troponins and NT-pro BNP) has been reported in chemotherapy naive patients with breast cancer, indicating that the presence of cancer can result in myocardial injury independent of the treatment and some of these peptides (e.g. copeptin) have been related to all-cause mortality.[29]

Anthracycline induced cardiotoxicity (AIC)

Anthracyclines are a class of antibiotics derived from the plant '*Streptomyces peucetius'*, a species of actinobacteria.[30] The four most common anthracyclines are doxorubicin, daunorubicin, epirubicin and idarubicin.[31]

The first anthracycline drug, daunorubicin was found to have anticancer activity in mice, which spurred its clinical use in the late 1960s for the treatment of leukaemia, lymphoma and solid tumors.[32] Soon after discovery, some of the patients treated with these otherwise highly potent anticancer drugs were noted to develop a major side effect – cardiotoxicity,[32] most notably in the form of a dose-dependent cardiomyopathy and heart failure.[33-39]

Based on duration, cardiotoxicity from anthracycline use can be classified into:

• Acute toxicity – this is rare and usually reversible, occurs during or within 2 weeks after anthracycline treatment, it is related to rapid intravenous administration of anthracyclines leading to depression of myocardial contractility. This manifests as vasodilatation, hypotension and cardiac dysrhythmias (e.g. supraventricular tachycardia, non-specific ST segment or T wave abnormality), pericardial myocarditis syndrome or acute left ventricular failure.[40]

• Subacute toxicity – this is uncommon, it develops several weeks after administration (< 1 year), manifesting as acute left heart failure, myocarditis, and pericarditis.[40]

• Chronic toxicity – this is the most common form of anthracycline induced cardiotoxicity, develops late during the course of therapy (>1 year) or shortly after its termination, manifesting as occult ventricular dysfunction (chronic dilated cardiomyopathy), congestive heart failure, and arrhythmia.[40]

• Delayed toxicity – this has been recently found in the survivors of childhood cancers treated with anthracyclines, develops about 10-15 years after the

Table 3: Summary of studies that have used STE to illustrate early myocardial injury during cancer chemotherapy.[12]

Study	Method	Number	Mean Age (yrs)	Treatment	Echo timing	Pre-treatment Echo (GLS)	Post-treatment Echo (GLS)
Stoodley et al. 2013.[81]	STE	78	52±10	Doxorubicin 81%, epirubicin 19%	Pre- and 1-week post-anthracycline, then at 6 and 12 months	-18.6±2.4%	-17.0±2.3% (1 week) -18.2 ± 2.2% (6 months)
Stoodley et al. 2011.[82]	STE	52	49±9	Doxorubicin 77% epirubicin 23%	Pre- and 1- week post-anthracycline	-17.8±2.1%	-16.3±2.0% (1 week)
Negish et al. 2013.[83]	STE	81	50±11	Trastuzumab, doxorubicin 46%, RT 62%	Pre-trastuzumab, and 6 and 12 months later	-20.7±2.6%	-18.3±2.1% (6 months)
Sawaya et al. 2012.[84]	STE	81	50±10	Doxorubicin, epirubicin, trastuzumab, RT 60%	Pre-anthracycline and at 3, 6, 9, 12, and 15 months	-21.0±2.0%	-19.0±2.0% (3 months)
Sawaya et al. 2011.[59]	STE	43	49±10	Doxorubicin, epirubicin, trastuzumab, RT 11.6%	Pre-anthracycline and at 3 and 6 months	-20.5±2.2%	-19.3±2.4% (3 months)
Fallah-Rad et al. 2011.[85]	STE	42	47±9	Epirubicin, doxorubicin, trastuzumab, RT 98%	Pre-anthracycline, Pre trastuzumab and at 3, 6, 9,12 months	-19.8±1.8%	-16.4±1.1% (3 months while on trastuzumab)

STE-*speckle tracking echocardiography*, RT-*radiotherapy*, GLS-*global longitudinal strain*

termination of treatment, characterized by restrictive process with decreased left ventricular (LV) compliance and a thin left ventricle.[40]

The mechanism of cardiotoxicity from anthracycline use is still not completely understood despite decades of continued research. The proposed mechanisms following extensive studies include:
1. Generation of reactive oxygen species[41],
2. Degradation of mitochondrial function and activation of proapoptotic pathways[41], and
3. Topoisomerase II inhibition causing double stranded break-induced apoptosis and altering transcription.[41]

Anthracyclines result in generation of cellular oxidative stress which has been proposed as a first step leading to myocyte cell death by the activation of Protein Kinase Pathway. Protein kinases {mitogen-activated protein kinases (MAPKs) and stress-activated protein kinases (SAPKs)} have been proposed as a cellular mediator linking anthracyclines to the apoptotic pathway.[42] Compared with other cell types in the body, cardiomyocytes contain high content of mitochondria (about 30% of cardiomyocyte volume) largely because of their high energy needs and thus are at especially high risk of anthracycline-induced injury.[43]

Risk factors for anthracycline cardiotoxicity

The greatest risk factor for anthracycline-induced cardiotoxicity is the cumulative dose.[44] In a retrospective analysis of 4,018 patients treated with doxorubicin, it was found that a weekly dose schedule was associated with significantly lower incidence of heart failure when compared to the usual 3-week schedule.[45] This is explained by the fact that weekly dose schedule is associated with lesser cumulative doses at the time of administration unlike the 3-weekly dose schedule which will require higher cumulative doses at each encounter. It was also noted that as the cumulative amount of doxorubicin increased, the risk of cardiotoxicity also increases.[45]

Combination and adjuvant chemotherapy regimens may potentiate cardiotoxicity through synergistic myocardial injury mechanisms. Cyclophosphamide is a cytotoxic alkylating chemotherapeutic agent, while trastuzumab is a targeted monoclonal antibody directed against HER2 receptors. Although trastuzumab is not traditionally classified as a cytotoxic agent, it is independently associated with reversible left ventricular dysfunction and may potentiate anthracycline-induced cardiotoxicity when used sequentially or concurrently.[46] Also the presence of conventional cardiovascular risk factors (e.g. hypertension, diabetes mellitus, and obesity) have been shown to increase the risk of anthracycline cardiotoxicity.[47] Other identified risk factors for anthracycline-induced cardiotoxicity include; extremes of age,[44, 45] female gender,[44, 45] and prior mediastinal radiation therapy.[44, 45]

Other classes of drugs causing cardiotoxicity and their risk factors

Beyond anthracyclines, several other classes of anticancer therapies used in breast cancer management have been associated with important cardiovascular toxicities.[19]

1. Taxanes, particularly paclitaxel and docetaxel, may cause sinus bradycardia, atrioventricular conduction abnormalities, ventricular ectopy, supraventricular arrhythmias, myocardial ischemia, and potentiation of anthracycline-induced cardiotoxicity. Risk factors for taxane-related cardiotoxicity include prior or concurrent anthracycline therapy, advanced age, pre-existing coronary artery disease, electrolyte abnormalities, cumulative chemotherapy exposure, and combination chemotherapy regimens.[48]
2. Human epidermal growth factor receptor-2 (HER2)-directed therapies such as trastuzumab and pertuzumab are associated with reversible left ventricular systolic dysfunction and heart failure due to interruption of HER2-mediated cardiomyocyte survival pathways.[49] Important risk factors for HER2 therapy-related cardiotoxicity include previous anthracycline exposure, older age, reduced baseline left ventricular ejection fraction, hypertension, diabetes mellitus, obesity, and prior chest irradiation. Sequential or concurrent use with anthracyclines substantially increases the risk of cardiac dysfunction.[19, 49]
3. Immune checkpoint inhibitors (ICIs), including programmed cell death protein-1 (PD-1), programmed death ligand-1 (PD-L1), and cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) inhibitors, have emerged as important causes of immune-mediated cardiovascular toxicity.[50] These agents may cause myocarditis, pericarditis, cardiac arrhythmias, vasculitis, stress cardiomyopathy, and heart failure.[50, 51] Although relatively uncommon, ICI-associated myocarditis carries high mortality when it occurs. Risk factors include combination immune checkpoint inhibitor therapy, pre-existing autoimmune disease, prior cardiovascular disease, diabetes mellitus, advanced age, and concurrent exposure to other cardiotoxic therapies.[51]
4. Tyrosine kinase inhibitors (TKIs), including lapatinib and other targeted kinase inhibitors, may induce hypertension, QT interval prolongation, myocardial ischemia, thromboembolic events, and left ventricular dysfunction.[52] Proposed mechanisms include endothelial dysfunction, mitochondrial injury, and impairment of myocardial survival signaling pathways.[52]

Risk factors for TKI-associated cardiotoxicity include uncontrolled hypertension, electrolyte disturbances, underlying ischemic heart disease, previous cardiac dysfunction, advanced age, and concomitant use of QT-prolonging medications.[52]

5. Cyclin-dependent kinase 4/6 (CDK4/6) inhibitors, particularly ribociclib, have also been associated with QT interval prolongation, arrhythmias, and occasional left ventricular dysfunction.[53] Risk factors include baseline prolonged QT interval, electrolyte abnormalities, hepatic dysfunction, concomitant administration of QT-prolonging drugs, and pre-existing cardiovascular disease.[53]

In general, several patient-related and treatment-related factors predispose individuals to cancer therapy-related cardiovascular toxicity. These include advanced age, female sex, pre-existing cardiovascular disease, hypertension, diabetes mellitus, dyslipidemia, obesity, smoking, chronic kidney disease, prior mediastinal radiation exposure, cumulative chemotherapy dose, high-dose chemotherapy regimens, and concurrent or sequential administration of multiple cardiotoxic agents.[19]

Detecting and monitoring for cardiotoxicity

Radionuclide ventriculography (RVG), Positron Emission Tomography (PET), Cardiac Magnetic Resonance (CMR), as well as echocardiography have been the proposed imaging methods for monitoring changes in cardiac structure and function during chemotherapy.[54] Other non-invasive methods includes the use of biomarkers such as different isoforms of troponin and cardiac natriuretic peptides.[55]

Despite the ability of noninvasive methods to detect myocardial dysfunction with chemotherapeutic agents, a tissue diagnosis remains the gold standard and this is obtained by an endomyocardial biopsy (EMB).[56]

Radionuclide ventriculography (RVG) was earlier considered to be the gold standard for cardiotoxicity screening,[57] however, a more recent meta-analysis showed that it overestimates LVEF and thus not accurate enough for heart failure prediction.[5] It is expensive, not readily available, and has a high risk of irradiation.

Positron emission tomography (PET) is useful for detection of metastasis and monitoring of response to chemotherapy, it has limited use in screening for cardiac dysfunction during chemotherapy.[58]

Cardiac magnetic resonance imaging (CMR) is considered the gold standard for the measurement of LVEF.[54] It has the potential to demonstrate subclinical myocardial changes prior to the onset of LV dysfunction because of its better soft tissue resolution and thus a unique possibility to demonstrate myocardial oedema seen in acute myocardial injury.[54] It is less used for routine screening and monitoring of cardiotoxicity because it is expensive and not readily available.

Echocardiography is probably the most readily available method to monitor cardiotoxicity, with serial measurements of the LVEF, valvular and pericardial involvement, and early detection of subclinical myocardial injury through the newest techniques (speckle tracking echocardiography).[59]

Although not specific, cardiac biomarkers including troponin[60] and natriuretic peptides[61] have been studied and found to be useful in diagnosis of chemotherapy-induced cardiotoxicity and in monitoring cancer therapy. They may also provide important information regarding the mechanism of cardiac dysfunction.

Standard 12-lead electrocardiogram (ECG) is cheap, readily available and has been reported to show different findings of cardiotoxicity such as sinus tachycardia, ST-T wave abnormalities, cardiac conduction disorders, QT prolongation, QRS voltage changes, and cardiac arrhythmia during chemotherapies in cancer patients.[62]

Use of speckle tracking echocardiography in early detection of myocardial changes during chemotherapy

Left ventricular ejection fraction appears to be the most clinically relevant parameter for the estimation of left ventricular function.[63] It is, however, not sensitive enough to detect subtle changes in the contractile function of the left ventricle and thus not suitable for detecting subclinical myocardial damage which may have major therapeutic and prognostic implications in a variety of clinical conditions.[63]

Speckle tracking echocardiography (STE) is a two-dimensional echo imaging analysis technique that studies the regional myocardial deformation.[64] This myocardial deformation is expressed as the percentage change from the original dimension. This is a dimensionless measurement and it is usually referred to as "strain".[65]

Speckle-tracking echocardiography is based on the frame-by-frame tracking of the natural acoustic markers of gray scale ultrasound images, or so-called "speckles", through the cardiac cycle. It is an angle-independent echo technique that allows for accurate assessment of segmental myocardial deformation along the direction of the wall and not along the ultrasound beam.[66] This allows for myocardial strain

along three spatial axes (longitudinal, circumferential and radial) according to the cardiac muscle physiology. Systolic myocardial deformation produces a longitudinal and circumferential shortening (resulting in a negative strain) and a radial thickening (resulting in a positive strain).[67]

Longitudinal strain is more reproducible than the radial and circumferential, also global strain has better reproducibility than the segmental strain.[68] The normal GLS is usually in the range of -16% to -18% or more (i.e. more negative), the circumferential strain is usually greater than the longitudinal strain with average values in excess of "20%, while the average radial strain is in the range of +40 to +60%.[69]

Six peer-reviewed publications, involving approximately 377 patients treated with anthracycline containing regimens, used speckled tracking echocardiography to detect early myocardial changes (Table 2.3). These studies showed that in the absence of a reduction in LVEF, a 2DSTE–measured reduction in peak systolic global longitudinal strain (GLS) between 9% and 19% seems to be common either during or immediately after anthracycline therapy.

Treatment and prevention of anthracycline cardiotoxicity

Currently, there are no guidelines specific for the management of anthracycline induced cardiotoxicity. However, the American College of Cardiology/ American Heart Association (ACC/AHA) and Heart Failure Society of America (HFSA) guidelines for treatment of heart failure is being followed. Close collaboration between the cardiologist and oncologist is strongly recommended in order to establish specific management for the patients.[70]

The following modalities have been studied and used in the treatment and prevention of anthracycline induced cardiotoxicity.

1. Modification of dosage schedule e.g. decreasing the cumulative dose of anthracyclines or administration of anthracyclines as infusions rather than as boluses are some measures which may help in reducing cardiac toxicity.[71] Studies have shown significantly lower rate of clinical HF with an infusion duration of 6 hours or longer compared with a shorter infusion duration in adults.[72] It should be noted, however, that there is no safe dose of anthracycline. Even doses as low as 100 mg/m^2 of epirubicin have been associated with reduced cardiac function.[73]

2. Use of analogues of anthracycline which are less toxic but more expensive (e.g. PEGylated liposomal doxorubicin) has been shown to decrease the cardiotoxicity of anthracycline, even at doses >500mg/m^2.[74] However, limited studies have shown no difference in cardiotoxicity between epirubicin and doxorubicin at equipotent doses.[75]

3. Cardio-protective agents e.g., dexrazoxane, an ethylene diamine tetraacetic acid (EDTA)-like chelator, may reduce the risk of cardiotoxicity in association with doxorubicin or epirubicin. Its use is limited to patients who receive a cumulative dose of doxorubicin >300 mg/m^2 or epirubicin >540mg/m^2.[76] Dexrazoxane has been approved by the United Staes food and drug administration (FDA) for mostly advanced breast cancer patients and has been shown to reduce the incidence of left ventricular dysfunction and heart failure.[77, 78]

The beta-adrenergic blockers (especially carvedilol), angiotensin converting enzyme inhibitors (ACEIs), and angiotensin receptor blockers (ARBs) have shown some protection against doxorubicin-induced left ventricular dysfunction through their antioxidant properties.[79, 80]

An antioxidant, probucol, has been shown to prevent the decrease in LVEF of doxorubicin cardiotoxicity in animal models but yet to be tried in humans.[79]

CONCLUSION

Anthracycline-based chemotherapy remains integral to breast cancer treatment but is associated with significant cardiotoxicity. Early detection using imaging and biomarkers is critical to preventing irreversible cardiac dysfunction. Risk stratification and timely cardioprotective interventions can improve outcomes. Strengthening cardio-oncology collaboration is essential. Integrating routine cardiovascular monitoring into cancer care will reduce long-term morbidity and mortality.

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