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abstract

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Asra Saeed, Jawaid Akhtar Mallick, Hiba Siddiqui, Khadija Mahar, Rimsha Shahid, Farrukh Ashraf, Asma Khan, Saad Jamal, Qurat ul Ain Badar

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Silent Shadows: Unraveling Radiotherapy-Induced Cardiotoxicity in Breast Cancer

Author: Asra Saeed[1], Jawaid Akhtar Mallick[1], Hiba Siddiqui[1], Khadija Mahar[1], Rimsha Shahid[1], Farrukh Ashraf[1], Asma Khan[1], Saad Jamal[1], Qurat ul Ain Badar[1]

Affiliation: [1]Department of Radiation Oncology, Dr. Ziauddin Hospital, Karachi, Pakistan

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Introduction: Breast cancer remains the most frequently diagnosed malignancy among women worldwide, with approximately 2 million new cases annually. Radiotherapy (RT) significantly reduces local recurrence and breast cancer related mortality; however, incidental irradiation of cardiac sub-structures can lead to radiation-induced heart disease (RIHD). Despite substantial advances in treatment planning and dose optimization, a considerable proportion of patients remain at risk of cardiac toxicity. Current evidence suggests a linear relationship between mean heart dose (MHD) and cardiac events, with an excess relative risk of approximately 4–7% per Gy increase in MHD.

This narrative review aims to establish evidence regarding dose-response relationships, cardiac substructure sensitivity, modern heart-sparing techniques, early detection strategies, and the balance between oncologic benefit and cardiovascular risk in breast cancer radiotherapy.

Methodology: A comprehensive literature search was conducted from January 2015 to September 2025 using the Cochrane Library, PubMed Central, and Google Scholar. Studies involving breast cancer patients treated with adjuvant radiotherapy to the breast/chest wall with or without regional nodal irradiation and reporting cardiac outcomes were included. Over 250 records were identified; after removal of duplicates and screening, 31 relevant studies were incorporated. Landmark randomized trials, meta-analyses, dosimetric studies, and prospective imaging-based investigations were narratively analyzed. The narrative review was synthesized across four domains: epidemiology and risk magnitude, dose-response relationships and substructure dosimetry, impact of modern RT techniques, and early cardiac injury detection and risk stratification.

Results: A consistent linear dose-response relationship between MHD and major coronary events was observed, with an excess MHD of approximately 7.4% per Gy. Radiotherapy was associated with a 6.4% increase in 10-year cardiovascular event risk. Randomized trial data by Taylor et al. demonstrated an excess relative risk of 0.04 per Gy for cardiac

mortality. Meta-analytic evidence showed that left-sided RT significantly increased the risk of coronary heart disease (RR 1.29) and cardiac death (RR 1.22) compared with right-sided RT. Cardiac substructures, particularly the left anterior descending artery (LAD) and left ventricle (LV), appeared more predictive of ischemic risk than whole-heart dose alone. Dosimetric studies demonstrated that deep inspiration breath-hold (DIBH) reduced LAD maximum and mean doses by 31.7% and 28.1%, respectively, compared with free-breathing plans ($p \leq 0.001$), supporting its routine clinical implementation. Advanced techniques such as VMAT achieved acceptable target coverage while facilitating cardiac dose reduction as compared to 3D-CRT. Although RT provides an absolute survival benefit of approximately 4–5% against breast cancer mortality, it is associated with a modest increase in cardiovascular mortality of about 0.2–0.3%, underscoring the importance of individualized risk–benefit assessment. Advanced echocardiographic techniques, including strain imaging, demonstrated early subclinical myocardial dysfunction within six months of RT, highlighting opportunities for early intervention.

Conclusion: This review provides an insight into the current prevalence of radiotherapy induced cardiotoxicity in breast cancer patients and most commonly used approaches to possibly alleviate the adverse effects of radiation. Despite clear evidence linking radiation induced cardiotoxicity, a clear consensus on dose constraints, radiotherapy volumes for cardiac sparing is required. Cardio-oncology, as an emerging multidisciplinary field might serve as a bridge in the current gaps of researches on cardio-protection and cardiotoxicity.

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