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The role of color doppler echocardiography in evaluating ventricular remodeling and cardiotoxicity following radiotherapy in thoracic cancer patients

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► ***Original article***

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ABSTRACT

Background: Radiotherapy (RT) for thoracic malignancies, such as breast and lung cancer, can induce cardiac injury, leading to ventricular remodeling and heart failure (HF), which negatively impacts long-term health outcomes. This study aimed to evaluate the effectiveness of color Doppler echocardiography in detecting early signs of ventricular remodeling and cardiotoxicity in patients undergoing thoracic RT. ***Materials and Methods:*** A retrospective analysis was performed on 80 patients with thoracic cancers who underwent RT between June 2022 and December 2024. Patients were divided into high-dose RT (n=49) and standard-dose RT groups (n=31). Serial color Doppler echocardiography was conducted before, immediately after, and at a 6-month follow-up to assess changes in cardiac structure and function. ***Results:*** Post-RT, both groups showed an increase in left ventricular end-diastolic volume index (LVEDVI), with the high-dose group showing significantly greater changes ($P<0.05$). Eleven patients in the high-dose group showed signs of HF, including increased left ventricular diameters and reduced ejection fraction (LVEF) ($P<0.05$). Color Doppler echocardiography demonstrated high sensitivity and specificity in detecting RT-related cardiotoxicity. ***Conclusion:*** Color doppler echocardiography is a valuable, non-invasive tool for monitoring ventricular remodeling and detecting early cardiotoxic effects of RT in thoracic cancer patients, enabling timely interventions and improved cardiac outcomes.

INTRODUCTION

Radiotherapy (RT) is a cornerstone in the treatment of various thoracic malignancies, including breast cancer, lung cancer, and mediastinal lymphomas [1]. Despite its proven efficacy in improving cancer-specific survival, RT carries the risk of unintended cardiovascular side effects, particularly radiation-induced heart disease (RIHD), which can compromise long-term quality of life and increase mortality in cancer survivors [2-4]. Among the most serious cardiac complications is ventricular remodeling, a pathological process that may culminate in heart failure (HF) if not identified and managed early [5, 6].

Ventricular remodeling encompasses a spectrum of structural and functional changes in the myocardium, such as chamber dilation, myocardial fibrosis, and reduced contractility [7]. These alterations often develop gradually and can remain subclinical for years following thoracic irradiation [8]. However, once remodeling becomes clinically apparent, it is frequently associated with poor cardiac outcomes and a significant decline in functional status [9]. As such, early detection of subclinical remodeling is essential to initiating timely therapeutic interventions and reducing the long-term cardiac burden in patients receiving RT [10, 11].

Currently, the clinical management of cardiotoxicity in thoracic cancer patients is hindered by the lack of standardized monitoring protocols and practical, cost-effective diagnostic tools for long-term follow-up [12]. Identifying patients at higher risk of cardiac dysfunction remains a challenge, particularly given that routine imaging modalities such as cardiac MRI, while precise, are often inaccessible or impractical for repeated use in large patient populations [13, 14].

Color Doppler echocardiography is a non-invasive, widely available imaging technique that offers real-time insights into cardiac morphology and function [15]. It allows for the measurement of ventricular dimensions, evaluation of wall motion abnormalities, estimation of ejection fraction, and assessment of intracardiac blood flow patterns [16]. Its portability, absence of radiation exposure, and capacity for serial evaluations make it an attractive option for long-term cardiac surveillance in patients undergoing RT.

Although echocardiography is frequently employed in general cardiology, its specific application in detecting early ventricular remodeling and heart failure in patients following thoracic RT has

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not been thoroughly investigated [17]. There is growing recognition that early echocardiographic changes-such as increases in left ventricular end-diastolic volume, alterations in systolic dimensions, and reductions in ejection fraction-can serve as early warning signs of cardiotoxicity [17]. Therefore, this study aims to evaluate the clinical value of color Doppler echocardiography in detecting ventricular remodeling and early heart failure in patients who have undergone thoracic radiotherapy. By comparing echocardiographic findings across different RT exposure levels and time points, we aim to highlight the utility of this modality in guiding proactive cardiac management, improving patient outcomes, and informing follow-up strategies in oncology care.

This study highlights the use of color Doppler echocardiography for early detection of ventricular remodeling and cardiotoxicity following thoracic radiotherapy. It provides new insights into the progression of RT-induced cardiac damage and its potential to predict heart failure, particularly differentiating the effects of high-dose versus standard-dose RT.

MATERIALS AND METHODS

Study design and patient selection

This retrospective observational study included 80 patients diagnosed with thoracic malignancies, consisting of lung cancer, breast cancer, and mediastinal lymphoma, who underwent radiotherapy (RT) at our institution between June 2022 and December 2024. Ethical approval was granted by the Institutional Ethics Committee of the Affiliated Rehabilitation Hospital of Nanchang University, Nanchang, China (approval number: SFYLL-KY-PJ-2025-055 2022-45). Informed consent was waived due to the retrospective nature of the study.

The inclusion criteria for this study required patients aged 18-80 years with thoracic malignancies who completed curative-intent thoracic radiotherapy. Patients must have undergone both baseline and follow-up color Doppler echocardiographic evaluations. Exclusion criteria included patients with pre-existing heart failure, cardiomyopathy, or severe valvular heart disease, as well as those with a history of myocardial infarction or recent coronary revascularization. Patients who were exposed to concurrent anthracyclines or other cardiotoxic chemotherapies were also excluded to isolate the effects of radiotherapy.

Among the 80 enrolled patients, 49 were classified into the high-dose RT group (HD-RT), which received a mean heart dose ≥10 Gy, and 31 patients were categorized into the standard-dose RT group (SD-RT), who received a mean heart dose <10 Gy.

Radiotherapy procedure

Radiotherapy was administered using a Varian TrueBeam® linear accelerator (Varian Medical Systems, USA) equipped with 3D conformal or intensity-modulated radiotherapy (IMRT) techniques. The radiation planning was performed using the Eclipse™ Treatment Planning System (Varian Medical Systems, USA). The treatment planning aimed to maximize tumor control while minimizing cardiac exposure. The total prescribed dose was 60 Gy in 30 fractions for both groups, delivered over six weeks, with the planning aimed to ensure that the heart received a mean dose of less than 10 Gy in the SD-RT group and ≥10 Gy in the HD-RT group. Cardiac dosimetry parameters, including mean heart dose, V20, and maximum dose to the left ventricle, were extracted from the treatment planning system for each patient (figure 1).

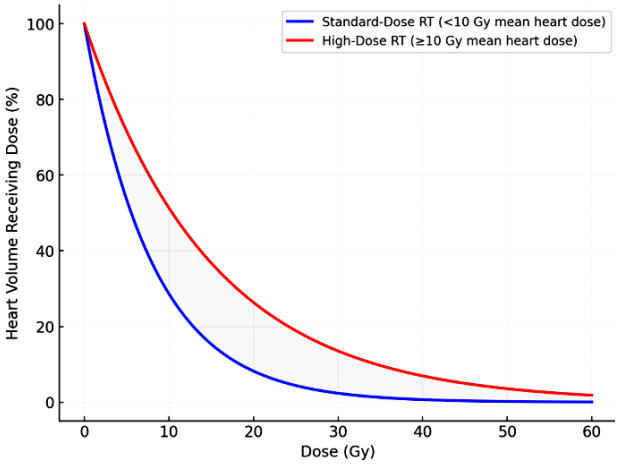

Figure 1. Dose–volume histogram (DVH) for heart in thoracic RT.

Color doppler echocardiography

Transthoracic echocardiography was performed using a Philips EPIQ 7C ultrasound system (Philips Healthcare, Netherlands) with an S5-1 transducer (1–5 MHz). The echocardiographic evaluations were conducted at four time points: within one week before starting radiotherapy (T1), immediately after completing radiotherapy (T2), 1 month after radiotherapy (T3), and 3 months after radiotherapy (T4). Two certified cardiologists performed the echocardiograms and analyzed the following parameters: left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), left ventricular end-diastolic volume index (LVEDVI), and left ventricular ejection fraction (LVEF). All measurements were averaged over three cardiac cycles during quiet respiration.

Radiation-induced cardiotoxicity and heart failure diagnosis

Radiation-induced cardiotoxicity was defined based on the presence of new or worsening systolic dysfunction (LVEF <50%) or adverse ventricular

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remodeling, including increased LVEDD or LVESD compared to baseline values. Clinical features such as dyspnea, fatigue, peripheral edema, and physical examination findings (e.g., pulmonary rales) were also considered for diagnosing heart failure. Diagnoses of cardiotoxicity and heart failure were independently confirmed by two cardiologists, with any discrepancies resolved by consensus.

Radiotherapy planning

Radiotherapy planning was conducted using the Eclipse™ Treatment Planning System (Varian Medical Systems, USA). The treatment technique employed was either 3D conformal radiotherapy or intensity-modulated radiotherapy (IMRT), depending on the patient's tumor characteristics. The radiation fields were carefully designed to focus on the tumor area while minimizing exposure to the heart and other healthy tissues. The goal was to deliver a dose of 60 Gy in 30 fractions, while keeping the cardiac dose below 10 Gy for the standard-dose group and exceeding 10 Gy for the high-dose group. A priority was given to ensuring that radiation was delivered to the cancerous regions with minimal collateral exposure to the heart.

Statistical analysis

Data were analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean ± standard deviation (SD) or median (interquartile range), based on their distribution. Comparisons between groups were performed using independent-samples t-tests or Mann–Whitney U tests for continuous variables and chi-square tests for categorical variables. For repeated measures, analysis of variance (ANOVA) with Bonferroni correction was used to compare echocardiographic parameters over time. The diagnostic performance of color Doppler echocardiography in detecting radiation-induced cardiotoxicity was assessed using receiver operating characteristic (ROC) curve analysis.

RESULTS

Baseline characteristics

A total of 80 patients with thoracic malignancies who completed curative-intent radiotherapy (RT) were included in this study. Based on cardiac radiation dose, patients were assigned to the high-dose radiotherapy group (HD-RT, n=49) or the standard-dose radiotherapy group (SD-RT, n=31). As summarized in table 1, there were no statistically significant differences between groups in terms of age, sex distribution, baseline cardiovascular risk factors (including hypertension, diabetes, and smoking history), or initial echocardiographic parameters. The mean age was 61.8 ± 9.7 years in the HD-RT group and 62.9 ± 10.2 years in the SD-RT group (p = 0.65). Baseline left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVEDD), and left ventricular end-systolic diameter (LVESD) were similar, confirming initial cardiac function comparability.

Table 1. Baseline characteristics of study population.

Parameter	HD-RT Group (n=49)	SD-RT Group (n=31)	p-value
Age (years)	61.8 ± 9.7	62.9 ± 10.2	0.65
Male, n (%)	33 (67.3%)	20 (64.5%)	0.79
Hypertension, n (%)	27 (55.1%)	16 (51.6%)	0.77
Diabetes mellitus, n (%)	18 (36.7%)	11 (35.5%)	0.91
Smoking, n (%)	26 (53.1%)	13 (41.9%)	0.33
Cancer type, n (%)	Lung: 26 (53.1%) Breast: 15 (30.6%) Lymphoma: 8 (16.3%)	Lung: 15 (48.4%) Breast: 10 (32.3%) Lymphoma: 6 (19.3%)	0.88
Stage distribution, n (%)	Stage II: 14 (28.6%) Stage III: 23 (46.9%) Stage IV: 12 (24.5%)	Stage II: 9 (29.0%) Stage III: 14 (45.2%) Stage IV: 8 (25.8%)	0.97
Tumor grade, n (%)	Low: 10 (20.4%) Intermediate: 26 (53.1%) High: 13 (26.5%)	Low: 6 (19.4%) Intermediate: 17 (54.8%) High: 8 (25.8%)	0.99
Baseline LVEF (%)	56.1 ± 5.8	55.6 ± 6.1	0.68
Baseline LVEDD (mm)	49.7 ± 4.3	50.1 ± 4.7	0.61
Baseline LVESD (mm)	33.8 ± 3.7	34.2 ± 3.6	0.54

LVEF = Left Ventricular Ejection Fraction, LVEDD = Left Ventricular End-Diastolic Diameter, LVESD = Left Ventricular End-Systolic Diameter, HD-RT = High-Dose Radiotherapy, SD-RT = Standard-Dose Radiotherapy.

Table 1 summarizes the baseline characteristics of the study population, comparing patients who received high-dose radiotherapy (HD-RT, mean heart dose ≥10 Gy) with those who received standard-dose radiotherapy (SD-RT, mean heart dose <10 Gy). Variables include demographic data (age, sex), cardiovascular risk factors (hypertension, diabetes mellitus, smoking status), oncologic features (cancer type, stage, and histological grade), and baseline echocardiographic parameters (LVEF, LVEDD, LVESD). Data are expressed as mean ± standard deviation for continuous variables and as number (percentage) for categorical variables. The p-values indicate statistical differences between the two groups.

Progression of ventricular remodeling post-radiotherapy

Serial echocardiographic evaluations at four time points (pre-RT [T1], post-RT [T2], 1-month [T3], and 3 months [T4]) (figure 2) revealed that the HD-RT group experienced significantly greater adverse ventricular remodeling compared to the SD-RT group (table 2).

In the HD-RT group, left ventricular end-diastolic volume index (LVEDVI) progressively increased from 61.9±6.2 mL/m^2 at baseline to 75.6±7.9 mL/m^2 at 3

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months (T4), whereas the SD-RT group exhibited only a modest increase to 67.4±6.8 mL/m^2 (p<0.001 at T4). LVEDD and LVESD followed similar patterns of enlargement, with significant group differences emerging from T2 onward. LVEF declined more sharply in the HD-RT group, reaching 48.1%±6.3% at T4 compared to 53.6% ± 5.8% in the SD-RT group (p=0.002).

Table 2. Serial echocardiographic parameters by group.

Parameter	Timepoint	HD-RT Group (mean ± SD)	SD-RT Group (mean ± SD)	p-value
LVEDVI (mL/m²)	T1	61.9 ± 6.2	62.4 ± 6.4	0.73
	T2	69.8 ± 6.9	64.6 ± 6.3	<0.001
	T3	72.2 ± 7.5	66.2 ± 6.6	<0.001
	T4	75.6 ± 7.9	67.4 ± 6.8	<0.001
LVEDD (mm)	T1	49.7 ± 4.3	50.1 ± 4.7	0.61
	T2	52.6 ± 4.8	50.8 ± 4.5	0.02
	T3	54.4 ± 5.0	51.7 ± 4.6	0.01
	T4	55.8 ± 5.2	52.0 ± 4.8	0.004
LVESD (mm)	T1	33.8 ± 3.7	34.2 ± 3.6	0.54
	T2	37.4 ± 4.0	35.0 ± 3.9	0.01
	T3	39.1 ± 4.3	35.4 ± 4.2	<0.01
	T4	40.5 ± 4.5	36.0 ± 4.1	<0.001
LVEF (%)	T1	56.1 ± 5.8	55.6 ± 6.1	0.68
	T2	52.7 ± 6.0	54.1 ± 6.2	0.19
	T3	50.1 ± 6.3	53.0 ± 5.9	0.04
	T4	48.1 ± 6.3	53.6 ± 5.8	0.002

LVEDVI = Left Ventricular End-Diastolic Volume Index, LVEDD = Left Ventricular End-Diastolic Diameter, LVESD = Left Ventricular End-Systolic Diameter, LVEF = Left Ventricular Ejection Fraction, HD-RT = High-Dose Radiotherapy, SD-RT = Standard-Dose Radiotherapy.

Table 2 shows serial measurements of key echocardiographic parameters (LVEDVI, LVEDD, LVESD, and LVEF) taken at four time points (T1: baseline, T2: post-radiotherapy, T3: 1-month post-RT, and T4: 3 months post-RT) for patients receiving high-dose radiotherapy (HD-RT) and standard-dose radiotherapy (SD-RT). The changes in these parameters are compared between the two groups, with statistical significance indicated by p-values.

Incidence and characteristics of radiation-induced heart failure

Heart failure (HF) developed in 13 patients (26.5%) in the HD-RT group during the 3-month follow-up. Comparisons within this group revealed that patients who developed HF had significantly greater increases in LVEDD and LVESD and more pronounced declines in LVEF by T4 compared to those without HF. For instance, mean LVEF decreased from 55.3%±5.4% to 40.8%±5.9% in the HF subgroup (p<0.001), whereas patients without HF showed only a mild reduction (from 56.6%±5.9% to 51.5%±5.7%, p=0.06).

Table 3, compares echocardiographic changes in patients receiving high-dose radiotherapy (HD-RT) who developed heart failure (HF) with those who did not. The parameters of interest-LVEDD, LVESD, and LVEF-are shown at two time points: baseline (T1) and 3 months post-RT (T4). The differences in these parameters between the two groups (HF vs. No HF) are shown, with statistical significance indicated by the p-values.

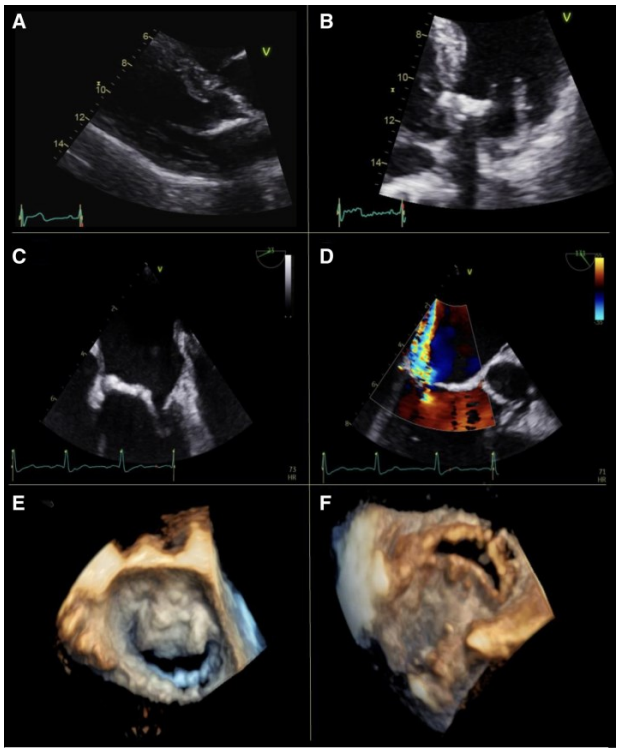

Figure 2. Echocardiographic findings in a 53-year-old woman who had previously received radiotherapy for lymphoma at the age of 42. Panels **A-C** (transthoracic and transesophageal echocardiography) reveal pronounced thickening and calcification of the basal anterior mitral leaflet and the aorto-mitral curtain. Panel **D** demonstrates a posteriorly directed jet of mitral regurgitation. Panels **E** and **F** show 4-dimensional reconstructions of the mitral valve, highlighting relative preservation of the leaflet tips and commissures, with panel **E** displaying a surgical perspective and panel **F** depicting the view from the left ventricle.

Table 3. Echocardiographic Changes in HD-RT Patients With vs. Without HF.

Parameter	HF (n=13)	No HF (n=36)	p-value (T4 comparison)
LVEDD (T1/T4)	50.9 ± 4.2 / 59.8 ± 4.7	49.3 ± 4.4 / 53.9 ± 4.6	<0.001
LVESD (T1/T4)	34.9 ± 3.8 / 44.7 ± 4.4	33.4 ± 3.5 / 38.6 ± 4.0	<0.001
LVEF (T1/T4)	55.3 ± 5.4 / 40.8 ± 5.9	56.6 ± 5.9 / 51.5 ± 5.7	<0.001

LVEF = Left Ventricular Ejection Fraction, LVEDD = Left Ventricular End-Diastolic Diameter, LVESD = Left Ventricular End-Systolic Diameter, HF = Heart Failure.

Diagnostic accuracy of color doppler echocardiography

Receiver operating characteristic (ROC) analysis showed strong predictive value of echocardiographic markers for detecting early radiation-induced HF, as shown in figure 3. The area under the curve (AUC) for a ΔLVEDVI increase ≥11.5 mL/m^2 was 0.88 (95% CI: 0.80-0.96; p<0.001), providing 84.6% sensitivity and 82.1% specificity. Similarly, an absolute LVEF reduction of >10% from baseline yielded an AUC of 0.86, with 81.3% sensitivity and 78.9% specificity.

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When combined, these two criteria produced an AUC of 0.91.

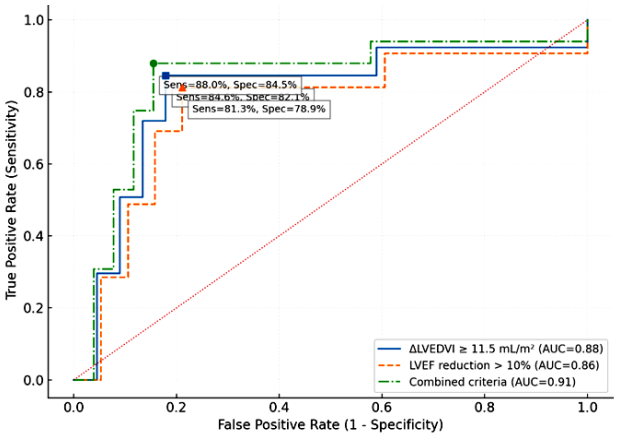

Figure 3. Receiver operating characteristic (ROC) curve for diagnostic accuracy of color doppler echocardiography in detecting radiation-induced cardiotoxicity.

Figure 3, illustrates the ROC curves for the diagnostic accuracy of color doppler echocardiography in detecting early radiation-induced cardiotoxicity in thoracic cancer patients.

DISCUSSION

This study evaluated the role of color doppler echocardiography in monitoring ventricular remodeling and detecting cardiotoxicity following thoracic RT in patients with thoracic cancers, including breast and lung malignancies. Our data demonstrated that patients receiving high-dose RT experienced significantly greater adverse ventricular remodeling, as shown by increased LVEDVI, LVEDD, and LVESD, accompanied by a decline in LVEF, compared to those receiving standard-dose. These echocardiographic changes correlated with clinical manifestations of HF in a subset of patients, highlighting the cardiotoxic potential of RT and underscoring the value of echocardiographic surveillance.

Radiotherapy-induced cardiac injury is a well-documented complication in thoracic malignancies, with effects ranging from subclinical myocardial damage to overt HF, ultimately impairing long-term survival and quality of life [18, 19]. The mechanisms underlying this injury involve direct myocardial cell damage, microvascular endothelial injury, inflammation, and progressive fibrosis, which together promote ventricular remodeling characterized by dilation, wall thinning, and systolic dysfunction [20, 21]. Our findings align with prior clinical and experimental studies demonstrating that the extent of myocardial remodeling and functional impairment is dose-dependent, with higher RT doses producing more pronounced cardiac effects [22, 23]. This emphasizes the critical importance of minimizing cardiac exposure during RT planning through advanced techniques such as intensity-modulated radiation therapy (IMRT) and proton therapy to mitigate long-term cardiac risks.

The significance of early detection of RT-induced cardiotoxicity cannot be overstated. Ventricular remodeling, particularly increases in LV volumes and reductions in LVEF, are established predictors of adverse cardiovascular outcomes, including symptomatic HF and mortality [24]. In our cohort, the ability of color Doppler echocardiography to detect these early changes prior to the onset of overt clinical symptoms allowed for identification of patients at increased risk for progression. This aligns with existing literature supporting echocardiography as a frontline, non-invasive modality for serial cardiac assessment in cancer patients undergoing potentially cardiotoxic therapies [25, 26].

Color Doppler echocardiography offers several advantages in this setting, including wide availability, cost-effectiveness, safety, and ease of repeatability, making it ideal for longitudinal monitoring [27]. Parameters such as LVEDVI, LVEDD, LVESD, and LVEF are well-established markers of remodeling and systolic function, and their serial measurement provides valuable insight into the temporal progression of myocardial injury. Moreover, the high sensitivity and specificity observed in detecting RT-related cardiotoxicity in our study reinforce its clinical utility as a diagnostic and prognostic tool.

While cardiac magnetic resonance imaging (CMR) remains the gold standard for volumetric and functional cardiac assessment, including tissue characterization, its routine use is limited by cost, availability, contraindications (e.g., implanted devices), and patient tolerability. Consequently, echocardiography continues to be the preferred modality in routine clinical practice, with the potential for integration of advanced echocardiographic techniques such as speckle-tracking strain imaging to enhance early detection of subtle myocardial dysfunction before changes in LVEF occur [28, 29]. Future research should explore the additive value of these novel techniques in RT-induced cardiotoxicity surveillance.

The clinical implications of our findings extend beyond diagnosis. Identification of early ventricular remodeling may prompt timely initiation of cardioprotective interventions, such as beta-blockers, ACE inhibitors, angiotensin receptor blockers, and mineralocorticoid receptor antagonists, which have been shown to attenuate remodeling and improve outcomes in HF of various etiologies [30]. Early echocardiographic detection of dysfunction could also influence RT planning and patient counseling, potentially leading to modification of RT dose or the use of protective agents such as dexrazoxane or antioxidants in high-risk patients [31, 32].

Despite these insights, our study has important

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limitations. The retrospective nature and single-center design limit the generalizability of the results. The relatively short follow-up period (6 months) may not capture the full spectrum of late cardiotoxic effects, which often manifest years after RT. Larger prospective studies with extended follow-up and inclusion of comprehensive clinical, biomarker, and imaging data are needed to better define the prognostic significance of echocardiographic findings and to establish standardized monitoring protocols. Additionally, the heterogeneous patient population with varying tumor types, stages, and concomitant therapies such as chemotherapy may introduce confounding factors affecting cardiac outcomes. Future investigations should aim to control for these variables and evaluate the interaction between multimodal cancer treatments and cardiac remodeling.

CONCLUSION

In conclusion, our study supports color doppler echocardiography as a valuable, non-invasive modality for early detection of ventricular remodeling and cardiotoxicity following thoracic radiotherapy in cancer patients. Regular echocardiographic surveillance facilitates identification of patients at risk for HF, enabling timely interventions that may improve cardiac outcomes and quality of life. Integration of echocardiography into routine post-RT follow-up protocols, combined with advances in RT techniques and cardioprotective strategies, holds promise for reducing the burden of RT-related cardiac morbidity.

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Conflict of interest: The authors declare no conflict of interest related to this study.

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Ethical considerations: This study was approved by the Institutional Ethics Committee of the Affiliated Rehabilitation Hospital of Nanchang University (approval number: SFYLL-KY-PJ-2025-055), and informed consent was waived due to the retrospective nature of the study.

Authors' contribution: X.P., X.X., and J.W., contributed to the conception and design of the study, data collection and analysis. J.W., wrote the first draft of the manuscript, with contributions from all authors. All authors reviewed and approved the final manuscript.

AI usage for manuscript preparation: No artificial intelligence tools were used in the preparation of this manuscript.

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