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Risk of cardiovascular-related death after radiotherapy for thoracic cancer

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Abstract

Cardiotoxicity following thoracic radiotherapy remains a critical issue, and this study aimed to assess the risk of Cardiovascular-Related Death (CVRD) after thoracic radiotherapy while comparing the risk of CVRD at different cancer sites. Data on patients with thoracic cancers treated with radiotherapy between 2000 and 2020 were analyzed, and the risk of CVRD was evaluated using death rates, Fine-Gray competing risks model, standardized mortality ratio (SMR), absolute excess risk (AER), and Cox regression to develop a predictive model. Patients receiving radiotherapy for thoracic cancer had a significantly increased risk of CVRD compared with the general population (Overall AER = 28.59, SMR = 2.37, 95% CI: 2.33–2.40). The risk of CVRD after radiotherapy was significantly lower in the right chest than the left (HR = 0.84, 95% CI: 0.79–0.89) and significantly higher in the left lower lung than in the upper (HR = 1.11, 95% CI: 1.01–1.22). A predictive model for the risk of CVRD in patients with left lower lung after radiotherapy was further constructed (C-index = 0.67, 95% CI: 0.67–0.68). The findings highlight that thoracic radiotherapy significantly increases cardiovascular disease risk, with patients with left lower lung cancer exhibiting the highest CVRD risk. A robust predictive model was developed, offering valuable insights for managing and predicting CVRD risk in thoracic malignancies.

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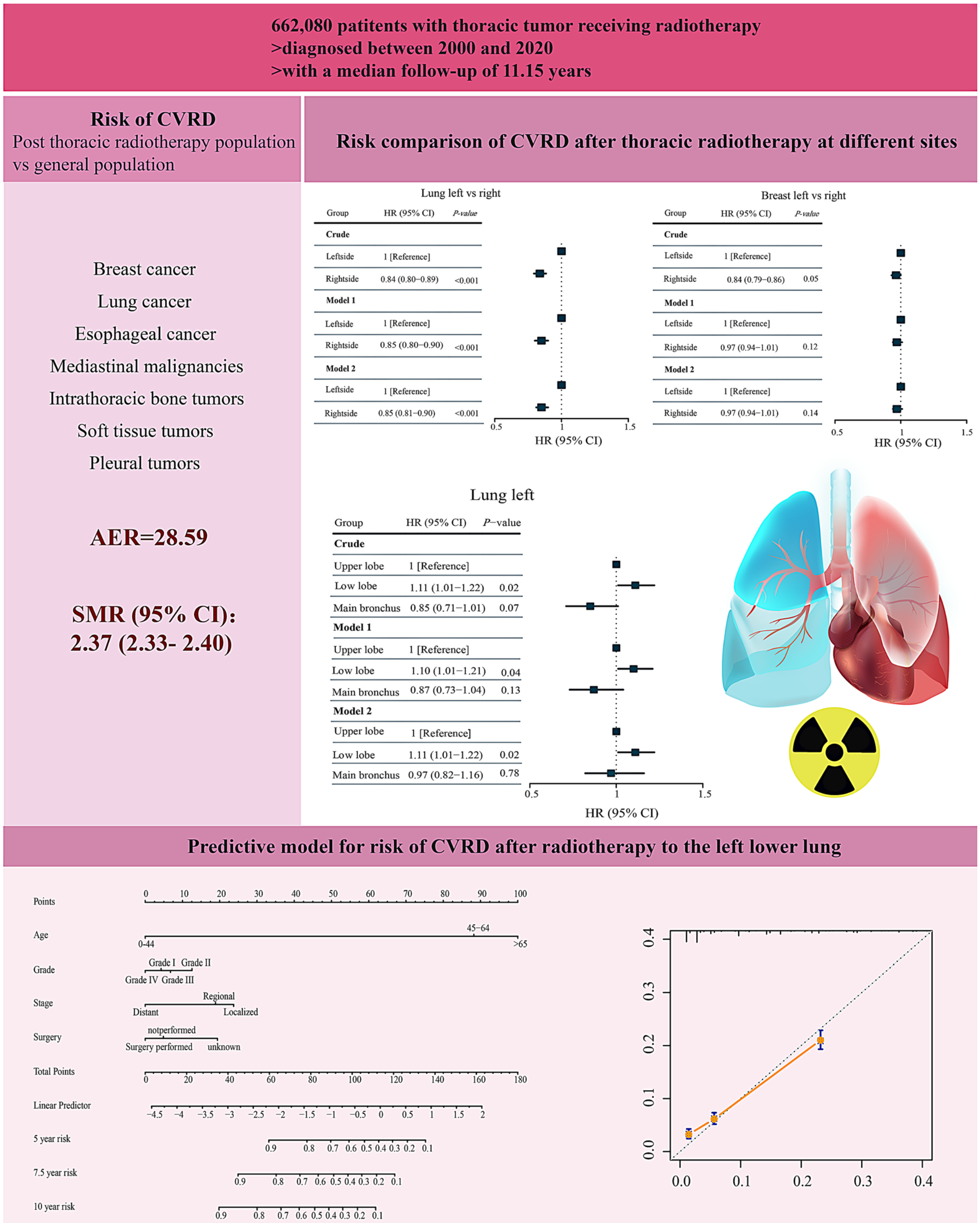
Graphical Abstract



This figure includes illustrations sourced from Freepik (https://www.freepik.com/), used under the applicable license terms. Proper attribution is provided as required. CVRD: Cardiovascular-Related Death.

Keywords CVRD, Thoracic cancer, Radiotherapy, Cardio-oncology

Novelty and Impact

This study is the first to systematically assess spatial CVRD risk distribution post-radiotherapy, identifying the left lower lung as the highest-risk region. The predictive model enhances personalized risk management, improving long-term outcomes for thoracic cancer patients.

Introduction

It is speculated that the number of new cases of major thoracic cancer in the United States will reach about 600,000 in 2024, accounting for more than 30% of the new cases of cancer in the United States [1]. So far, thoracic cancer remains a serious human health problem. Radiotherapy is an important treatment for malignant tumors. A significant proportion of various thoracic cancer, including lung, esophageal, and breast cancers, are indicated for radiotherapy at some stage of treatment. Radiotherapy has greatly improved the prognosis of various tumors [2]

However, thoracic radiotherapy inevitably increases the risk of cardiotoxicity, about 20% of lung cancer patients receiving radiotherapy experience cardiac injury [3]. When the heart is in the radiation field, it may lead to a variety of cardiovascular-related diseases, including myocardial infarction, valvular heart disease, and heart failure [4, 5]. Patients with thoracic cancer have a significantly increased risk of Cardiovascular-Related Death (CVRD) following radiotherapy [6–8]. Cardiovascular toxicity after radiotherapy can be effectively mitigated through timely intervention [9–11]. Therefore, it is necessary and meaningful to further understand cardiotoxicity after thoracic radiotherapy and identify high-risk groups for CVRD after radiotherapy.

Previous studies have reported that lowering the radiation dose received by the heart is essential for reducing the risk of CVRD following thoracic radiotherapy, as higher doses have been directly linked to increased CVRD risk [12–18]. However, the results of these studies tend to have some guiding significance only for individual patients in terms of Organ at Risk (OAR) dose constraints for radiotherapy target delineation. At the epidemiological level, the effects of factors such as age, tumor stage, and underlying diseases on CVRD risk after radiotherapy have been reported by several studies [19–23], but there are not many studies to investigate the differences in cardiovascular-related mortality risk after radiotherapy for thoracic cancer at different sites. Several studies indicated that radiotherapy to the left chest is associated with a significantly higher risk of CVRD compared to the right chest [24], but further more refined differences in the risk of radiotherapy and CVRD between chest anatomy have not been clarified by the results of the study. Further analysis of refined CVRD risk differences after radiotherapy between thoracic regions is crucial for managing CVRD risks in the broader post-radiotherapy population. We conducted a comprehensive analysis using the SEER database to explore the association between radiotherapy and cardiovascular death in patients with thoracic malignancies. This study aims to achieve three objectives: (1) assess the overall impact of thoracic radiotherapy on CVRD risk in patients with thoracic cancer, (2) compare CVRD risk differences across different tumor sites after treatment, and (3) identify and characterize high-risk subgroups, particularly those in high-risk regions. This study seeks to provide a scientific foundation for developing effective risk management strategies to address cardiovascular death in survivors of thoracic malignancies following radiotherapy.

Methods

Data source

Data for thoracic cancer patients were extracted from the Surveillance, Epidemiology, and End Results (SEER) project, a publicly accessible and authoritative database (Supplementary Methods). As the data were obtained from a public database, ethical approval was not required [25]

Study population

The inclusion criteria for the cohort were as follows: a. pathologically confirmed thoracic cancer [breast, lung, esophagus, mediastinum, Bone (ribs, sternums, clavicles and joints), pleura and soft tissues including the heart]; b. single primary cancer type; c. receiving radiotherapy; exclusion criteria were as follows: a. unknown cause of death; b. no active follow-up and definite follow-up time. We identified seven thoracic cancer patients according to the International Classification of Disease-10 (ICD-10), and the coding and names of the seven cancer types are shown in Supplementary Table 1.

Patient variables, follow-up and outcome setting

Patient variables included age at diagnosis (0–44 years, 45–64 years, and 65+ years), sex (male, female), race (White, Black, others), year of diagnosis (≤2010, >2010), cancer site [breast, lung, esophagus, mediastinum, bone (ribs sternums, clavicles and joints), pleura and soft tissue], tumor characteristics (grade and stage), years after diagnosis (<1 year, 1–3 years, 3–5 years, 5–10 years, 10–15 years, ≥15 years), and marital status (married, unmarried, unknown). The follow-up period for this study was set from the time of cancer diagnosis to death or follow-up cutoff, and the follow-up cutoff was 31 December 2020. The endpoint event for this study was defined as death from cardiac disease (coded according to ICD-10 classification: I20–I25).

Construction and verification of risk model

We randomly divided the left lower lung data from the SEER database into training and validation sets [26] (7:3 ratio) using R package caret. Fine-Gray competing risks regression (cmprsk) was employed to evaluate CVD risk factors (age, sex, race, marital status, stage, and diagnosis year) through univariable and multivariable analyses. A prognostic nomogram (rms) was developed to predict 5-/7.5-/10-year risks, with model performance assessed via calibration curves and time-dependent ROC analysis (riskRegression). All analyses used R v4.2.2.

Statistical analysis

Statistical analyses were performed using SPSS and R-studio. The risk of cardiac disease-related mortality was assessed using a Fine-Gray competing risks model (with all non-cardiac deaths treated as competing risks), and reported metrics included the Standardized Mortality Ratio (SMR, defined as the observed-to-expected deaths ratio) [27], Absolute Excess Risk (AER, calculated as: AER = 10,000 ×([number observed − number expected]/[person-years at risk]) [28], Hazard Ratio (HR), and 95% Confidence Interval (CI) [25]. The observed deaths represented the total cardiac disease-specific mortality from 2000 to 2020, while the expected deaths were calculated by multiplying person-years in the study cohort by the cause-specific mortality rates of the U.S. general middle-aged population, derived from CDC WONDER database (https://wonder.cdc.gov/) [29, 30] $p < 0.05$ was set to cons ider a statistical difference.

Results

Patient characteristics

Of the 662,080 patients with 7 intrathoracic malignancies identified, 423,367 (63.9%) had breast cancer, 208,922 (31.6%) had lung cancer, 29,149 (4.4%) had esophageal cancer, 322 had mediastinal malignancies, 203 had intrathoracic bone tumors, 74 had soft tissue tumors, and 43 had pleural tumors. Patient demographics and baseline clinical characteristics are presented in Table 1. The median follow-up time was 8.08 years [interquartile range (IQR) 3.67–13.67 years].

Analysis of CVRD risk in thoracic radiotherapy patient

Patients who underwent radiotherapy for thoracic cancer had a significantly increased risk of CVRD compared with the general population (Overall AER = 28.59, SMR = 2.37, 95% CI: 2.33–2.40). Subgroup analyses revealed that these increased risks were consistent across various time points following diagnosis: at 1-year post-diagnosis (AER = 37.84, SMR = 2.81, 95% CI: 2.71–2.91), while at 15 years (AER = 63.83, SMR = 4.06, 95% CI: 3.84–4.82). Specifically, patients with breast cancer had a significantly increased risk of CVRD compared with the general population (AER = 14.78, SMR = 1.71, 95% CI: 1.68–1.74), lung cancer patients had a significantly increased risk of CVRD compared with the general population (AER = 144.33, SMR = 7.91, 95% CI: 7.70–8.12), while esophageal cancer patients had a significantly increased risk of CVRD compared with the general population (AER = 156.35, SMR = 8.49, 95% CI: 7.98–9.02). Further analysis across subgroups revealed that patients with overall mediastinal tumors had a significantly increased risk of CVRD compared with the general population (AER = 1.78, SMR = 1.09, 95% CI: 0.22–3.17), thoracic bone tumors had a significantly increased risk of CVRD compared with the general population (AER = 5.51, SMR = 1.26, 95% CI: 0.25–3.70), and those with thoracic soft tissue tumors had a significantly increased risk of CVRD compared with the general population (AER = 142.49, SMR = 7.82, 95% CI: 0.88–28.24).

Table 1 Baseline characteristics of thoracic cancer patients receiving radiotherapy

Characteristics	n	%
Overall	662,080	100
Age at diagnosis		
0–44 years	61,068	9.2
45–64 years	320,784	48.5
65+ years	280,228	42.3
Race		
White	534,353	80.7
Black	69,235	10.5
Other*	56,141	8.5
Unknown	2,351	0.4
Sex		
Male	140,576	21.2
Female	521,504	78.8
Marital status		
Marital	380,336	57.4
Unmarried	258,179	39.0
Year of diagnosis		
≤2010	305,953	46.2
2010	356,127	53.8
Cancer site		
Breast	423,367	63.9
Lung	208,922	31.6
Esophagus	29,149	4.4
Mediastinum	322	0.0
Bone*	203	0.0
Soft Tissue	74	0.0
Pleura	43	0.0
Grade		
I	80,127	12.1
II	168,896	25.5
III	167,135	25.5
IV	13,674	2.1
Unknown	232,248	35.1
SEER stage		
Localized	292,323	44.2
Regional	208,165	31.4
Distant	155,514	23.5
Unknown	6,078	0.9
Surgery		
Yes	442,487	66.8
No	217,678	32.9
Unknown	1,915	0.3
Chemotherapy		
Yes	304,046	45.9
No evidence	358,034	54.1

Other* include American Indian/Alaska Native and Asian/Pacific Islander; Bone* include ribs sternums, clavicles and joints

The main results of SMR and AER are shown in Table 2. Subgroup analyses of the overall post-radiotherapy cohort, stratified by age, sex, race, disease stage, primary site, and surgical status, consistently demonstrated a trend toward higher cardiovascular-related death (CVRD) risk compared with the general population. Detailed results are presented in Supplementary Table 2.

Comparison of CVRD after radiotherapy in different parts of chest

We compared the risk of CVRD following radiotherapy for tumors in the left and right thoracic regions. The risk of CVRD after radiotherapy was significantly lower in the right chest than the left (HR = 0.85, 95% CI: 0.80–0.90; Fig. 1A). In contrast, no significant differences in CVRD risk were observed between left- and right-sided breast cancer patients following bilateral radiotherapy (Fig. 1B).

Subgroup analyses for lung cancer revealed a consistently higher CVRD risk for left-sided tumors compared to right-sided tumors across various patient characteristics. This trend was particularly pronounced among Caucasian patients, who exhibited a significantly lower CVRD risk with right-sided radiotherapy (HR = 0.85, 95% CI: 0.80–0.90). Similar trends were noted among Black patients and those of other races, though the differences were not statistically significant. Subgroup analyses based on the year of diagnosis further supported these findings, showing reduced CVRD risk for right-sided lung cancer in both the ≤2010 (HR = 0.81, 95% CI: 0.75–0.87) and > 2010 (HR = 0.91, 95% CI: 0.83–0.99) cohorts (Supplementary Fig. 1).

The association of lower CVRD risk with right-sided radiotherapy was consistent in both male (HR = 0.86, 95% CI: 0.80–0.92) and female (HR = 0.83, 95% CI: 0.76–0.91) patients. Additionally, age-stratified analyses showed significant reductions in CVRD risk for patients aged 45–64 years (HR = 0.76, 95% CI: 0.68–0.84) and those aged 65+ years (HR = 0.89, 95% CI: 0.83–0.95). However, no significant difference was observed in patients younger than 45 years (Supplementary Fig. 2).

In breast cancer, subgroup analyses based on age, sex, race, and year of diagnosis suggested a trend toward lower CVRD risk with right-sided radiotherapy compared to left-sided radiotherapy. However, these differences were not statistically significant (Supplementary Figs. 3–4).

For esophageal cancer, which is anatomically divided into upper, middle, and lower segments, no significant differences in CVRD risk were observed among patients receiving radiotherapy for tumors in these regions (Supplementary Fig. 5). Subgroup analyses stratified by sex, race, age, and year of diagnosis also showed no significant differences in CVRD risk between esophageal segments (Supplementary Fig. 6–7).

Table 2 AER and SMR for CVRD in patients with seven types of thoracic tumors receiving radiotherapy based on years after diagnosis

Cancer	Overall		Years After Diagnosis[#]											
			<1		1–3		3–5		5–10		10–15		15+	
	AER	SMR (95% CI)	AER	SMR (95% CI)	AER	SMR (95% CI)	AER	SMR (95% CI)	AER	SMR (95% CI)	AER	SMR (95% CI)	AER	SMR (95% CI)
Overall	28.59	2.37 (2.33- 2.40)	37.84	2.81 (2.71–2.91)	18.81	1.90 (1.84–1.97)	17.22	1.82 (1.75–1.90)	26.09	2.25 (2.19–2.32)	43.21	3.07 (2.96–3.18)	63.83	4.06 (3.84–4.28)
Breast	14.78	1.71 (1.68–1.74)	−9.71	0.54 (0.49–0.59)	−0.50	0.98 (0.93–1.03)	6.77	1.32 (1.26–1.39)	20.02	1.96 (1.90–2.02)	40.2	2.92 (2.82–3.03)	62.05	3.97 (3.76–4.19)
Lung	144.33	7.91 (7.70–8.12)	151.21	8.24 (7.90–8.59)	130.92	7.27 (6.91–7.64)	139.32	7.67 (7.09–8.29)	160.30	8.67 (8.02–9.37)	159.67	8.64 (7.38–10.06)	141.29	7.76 (5.38–10.85)
Esophagus	156.35	8.49 (7.98–9.02)	188.74	10.04 (9.10–11.05)	131.12	7.28 (6.43–8.21)	142.51	7.82 (6.54–9.29)	139.87	7.7 (6.50–9.05)	156.99	8.52 (6.45–11.03)	216.93	11.39 (6.95–17.58)
Mediastinum	1.78	1.09 (0.22–3.17)	20.64	1.99 (0.03–11.06)	12.20	1.58 (0.02–8.81)	-	- (-)	-	- (-)	1.54	37.17 (0.04–15.47)	-	- (-)
Bone*	5.51	1.26 (0.25–3.70)	38.14	2.83 (0.04–15.72)	16.68	1.80 (0.02–10.00)	32.49	2.56 (0.03–14.22)	-	- (-)	-	- (-)	-	- (-)
Soft Tissue	142.49	7.82 (0.88–28.24)	172.66	9.27 (0.12–51.)	-	- (-)	576.13	28.58 (0.37–159.04)	-	- (-)	-	- (-)	-	- (-)

The time interval does not include the upper limit. Abbreviations: CVRD, Cardiovascular-Related Death; CI, confidence interval; AER, Absolute Excess Risk; SMR, standardized mortality ratio; Bone* include ribs sternums, clavicles and joints

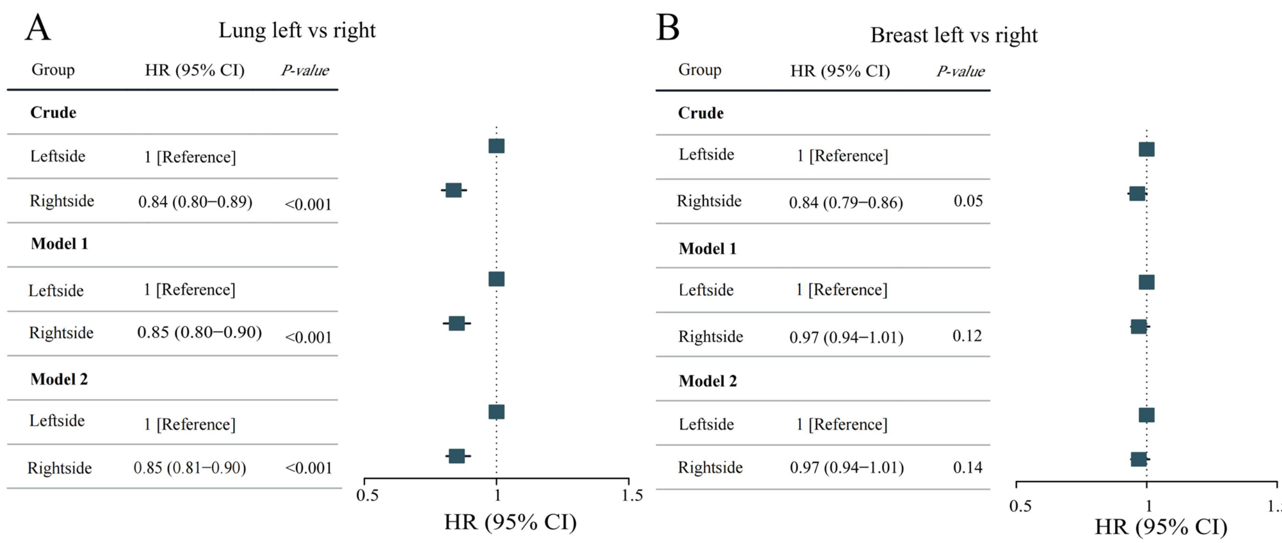


Fig. 1 **A**, CVRD risk control after left and right radiotherapy in the overall cohort of lung cancer; **B**, CVRD risk control after left and right radiotherapy in the overall cohort of breast cancer. (hr: hazard Ratio; $p < 0.05$)

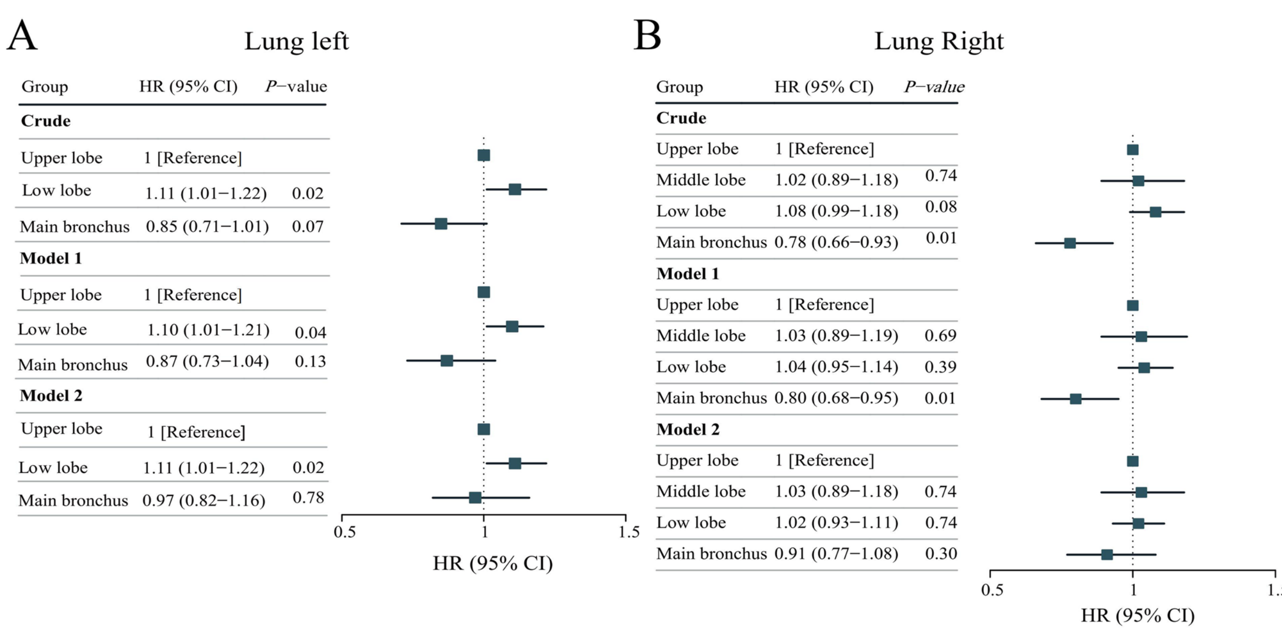


Fig. 2 **A**, comparison of CVRD risk after radiotherapy in different regions of the left lung; **B**, comparison of CVRD risk after radiotherapy in different regions of the right lung. (hr: hazard Ratio; $p < 0.05$)

Risk difference of CVRD after radiotherapy in different lobes of the left lung

Further analysis of CVRD risk in detailed anatomical substructures revealed that the risk of CVRD after radiotherapy was significantly higher in the left lower lung than in the upper (HR = 1.10, 95% CI: 1.01–1.21; Fig. 2A). Although there was a trend toward reduced CVRD risk in the left main bronchus relative to the left upper lobe, this difference was not statistically significant. In the right lung, the main bronchus showed a significantly lower CVRD risk compared to the right upper lobe, while no significant differences were observed among the upper, middle, and lower lobes (Fig. 2B).

Subgroup analyses for the left lung showed that patients aged 65+ years (HR = 1.12, 95% CI: 1.02–1.24) and White patients (HR = 1.12, 95% CI: 1.02–1.24) had a significantly higher CVRD risk with tumors in the left lower lobe compared to the left upper lobe. Although most other demographic groups exhibited a trend toward lower CVRD risk in the left upper lobe, these findings were not statistically significant (Supplementary Figs. 8–9).

In the right lung, male patients, individuals aged 65+ years (HR = 0.74, 95% CI: 0.59–0.92), White patients (HR = 0.74, 95% CI: 0.61–0.90), and those diagnosed between 2000 and 2010 (HR = 0.79, 95% CI: 0.63–0.98) showed significantly lower CVRD risk with radiotherapy for tumors in the right lower lobe compared to the right upper lobe. Other subgroups exhibited similar trends, though these were not statistically significant (Supplementary Figs. 10–11).

Based on these findings, the left lower lobe was identified as the highest-risk region for CVRD following thoracic radiotherapy.

A comparison of CVRD risk between the inner and outer quadrants of the left and right breast revealed a higher risk in the right outer quadrant compared to the left, though the difference was not statistically significant (Supplementary Fig. 12).

A cardiovascular disease (CRVD) risk assessment model for patients receiving left lower lobe radiotherapy

To evaluate risk factors for CVRD after thoracic radiotherapy, we developed a Fine-Gray model incorporating age, sex, race, stage, diagnosis year, surgical conditions and grade as predictors. Univariate and multivariate analyses identified seven significant factors (Supplementary Table 3), of which four (age, stage, surgical conditions and grade) were selected to construct the final prediction model. A nomogram (Fig. 3A) visualized 5-, 7.5-, and 10-year CVRD risks. The calibrated model achieved a C-index of 0.67 in the training cohort, demonstrating moderate discriminative ability. Calibration curves (Fig. 3B) and ROC analyses (Fig. 4A–B) further validated its accuracy in both training and test sets.

Discussion

This study conducted a retrospective analysis of a large cohort of thoracic cancer patients who underwent radiotherapy in the United States over a 20-year period. We investigated the relationship between thoracic radiotherapy and CVRD from multiple angles. Our findings indicated that all thoracic cancer patients receiving thoracic radiotherapy exhibited a significantly elevated overall CVRD risk in comparison to the general population. Notably, patients who received targeted radiotherapy to the thoracic left lower lung demonstrated the highest CVRD risk. Furthermore, we developed a predictive model to estimate CVRD risk in individuals with varying characteristics following radiotherapy to the left lower lung.

Our study systematically evaluated the spatial distribution of CVRD risk after thoracic radiotherapy, revealing significantly higher CVRD incidence in left-sided versus right-sided chest irradiation. Existing literature has well-documented that thoracic radiotherapy confers increased Cardiovascular Disease（CVD） risk in thoracic cancer patients [31, 32] with pathophysiological mechanisms involving radiation-induced endothelial dysfunction and vascular inflammation [32–37]. Notably, dose-optimized radiotherapy regimens have demonstrated significant cardioprotection, reducing both cardiotoxicity and cardiovascular mortality rates [13–18, 38], Clinical risk stratification should also consider comorbidities including advanced age, tumor staging, pre-existing CVD, and endocrine disorders [19–23]. Controversies persist regarding laterality-specific CVRD risks, some studies have shown that the risk of cardiovascular injury after radiotherapy for left thoracic tumors is significantly higher than that for right thoracic tumors [39–41], while others have shown that there is no significant difference in the risk of cardiovascular injury after radiotherapy for bilateral thoracic tumors [17, 42]. Based on this contradiction, our study identified a significantly higher CVRD after radiotherapy in the left chest than in the right chest by performing multiple statistical analyses and multiple subgroup analyses of a large sample size of thoracic tumors.

Our study systematically analyzed the spatial distribution of CVRD risk following thoracic radiotherapy, identifying the left lower lung as the most susceptible anatomical region. This observation is consistent with previous evidence demonstrating that minimizing radiation dose to the heart significantly improves CVRD outcomes in thoracic cancer patients [13–18, 38]. Notably, existing investigations have primarily focused on laterality-based cardiotoxicity comparisons, while our study advances this framework through high-resolution anatomical stratification of radiation-exposed areas. Further, for the first time, we constructed a post-radiation CVRD assessment model focusing on the areas at highest risk of CVRD following thoracic radiotherapy to more precisely localize the characteristics of the population at highest risk following thoracic radiotherapy.

As previously mentioned, our study exhibits several notable advantages compared with similar studies. Firstly, the analysis conducted on a large sample-sized cohort ensures the highly reliable and robust nature of our analytical results. Moreover, the implementation of extensive subgroup analyses enables us to conduct a more comprehensive assessment of cardiotoxicity.

However, since the data are based on the SEER database, our study has several limitations. First, the SEER database lacks detailed radiotherapy treatment parameters, including radiotherapy dose and specific radiotherapy techniques, which are essential for evaluating the risk of cardiotoxicity. In addition, the lack of detailed data in the SEER database on smoking status, pre-existing cardiovascular/metabolic comorbidities (hypertension, dyslipidemia, and diabetes), and certain systemic therapies

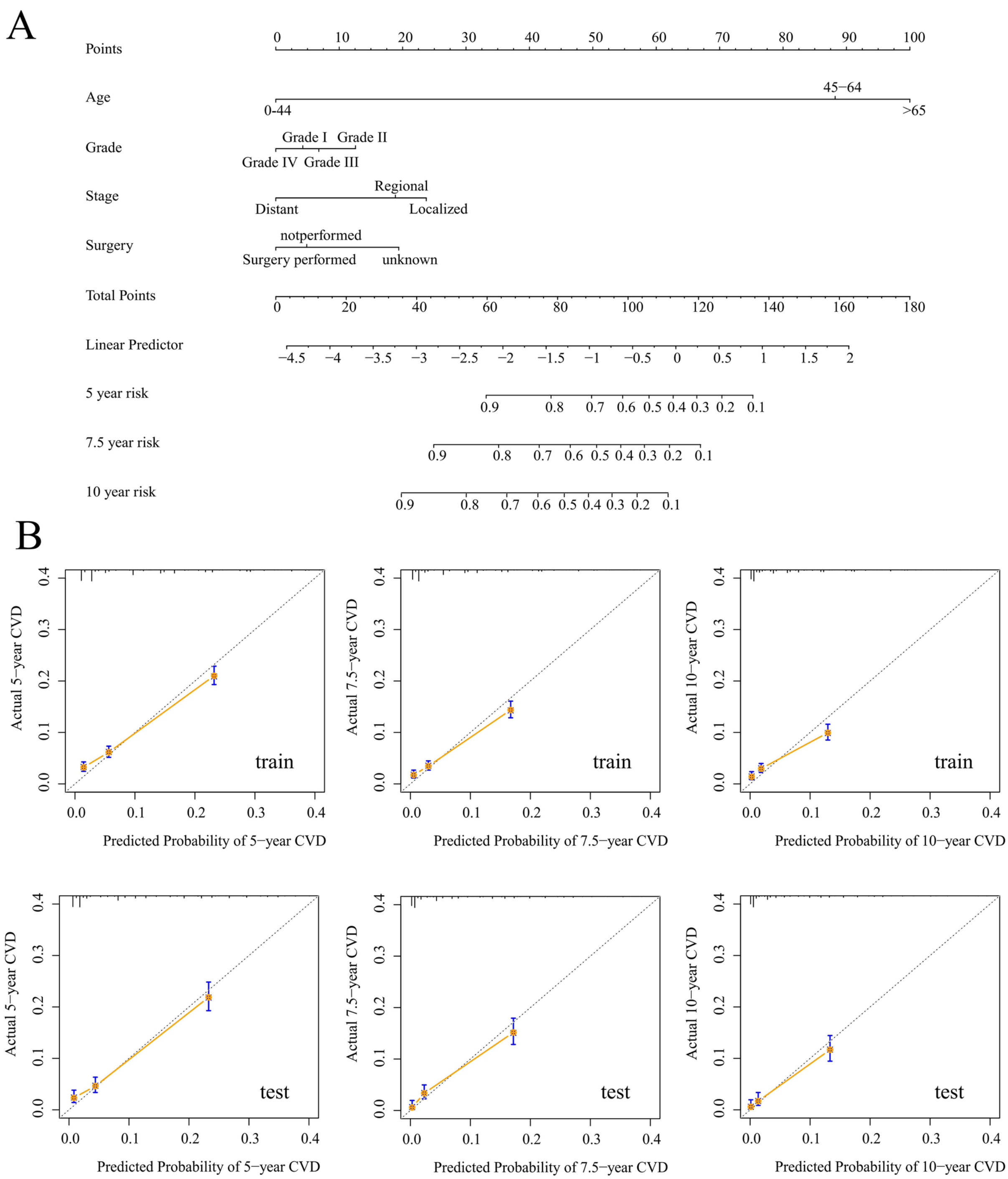


Fig. 3 **A**. Nomogram based on the 4-variable fine-gray competing risks model. **B**. Calibration curves for 5-, 7.5-, and 10-year predictions in training and validation sets of the 4-variable fine-gray model

precluded further analysis of their effects on cardiovascular disease (CVD) mortality risk. Finally, due to limitations in diagnostic coding in the SEER database, this study was unable to classify cardiac complications after radiotherapy (e.g. cardiomyopathy, coronary artery disease, pericardial disease, or valvular disease) into more detailed subtypes, which may have resulted in studies that could not distinguish between independent risks of different cardiac complications and limited the precision of clinical guidance.

Our study demonstrates the increased incidence of CVRD after thoracic radiotherapy, and attention should be paid to the cardiovascular health of patients during thoracic perioperative and for a long time after

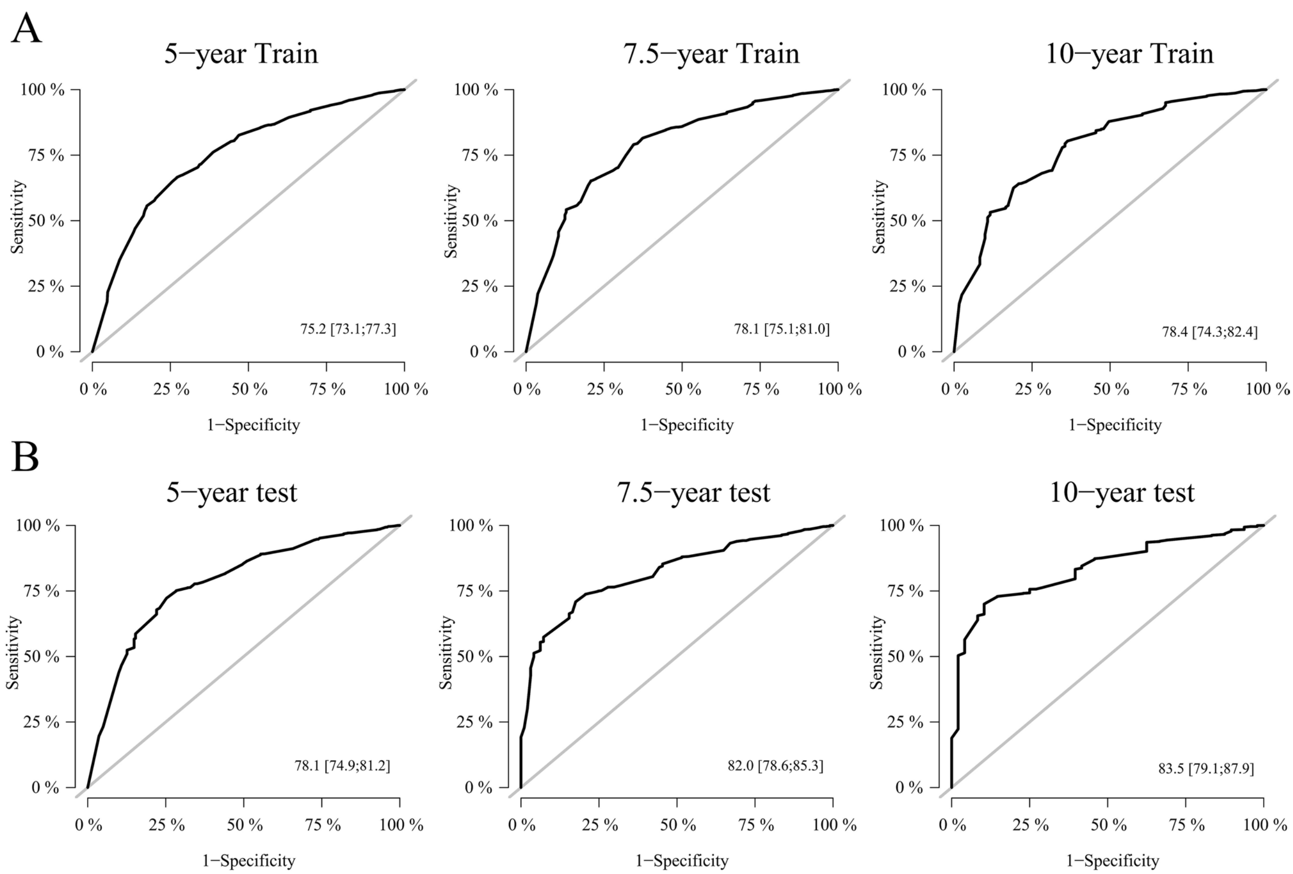


Fig. 4 **A**. Training set calibration at 5-, 7.5-, and 10-year timepoints, demonstrating agreement between predicted (x-axis) and observed (y-axis) cardiovascular disease risk. **B**. Validation set calibration at corresponding intervals, with dashed lines representing ideal prediction and solid lines showing model performance. ($p < 0.05$)

radiotherapy and try to avoid the emergence of CVRD. Among thoracic cancer, left lower tumors had the highest risk of CVRD after radiotherapy. It is suggested that CVRD in patients with left lower thoracic cancer after radiotherapy should be emphasized in clinical work.

Supplementary information

The online version contains supplementary material available at https://doi.org/10.1186/s13014-025-02770-0.

Supplementary Material 1

Supplementary Material 2: Supplementary Figure 1

Supplementary Material 3: Supplementary Figure 2

Supplementary Material 4: Supplementary Figure 3

Supplementary Material 5: Supplementary Figure 4

Supplementary Material 6: Supplementary Figure 5

Supplementary Material 7: Supplementary Figure 6

Supplementary Material 8: Supplementary Figure 7

Supplementary Material 9: Supplementary Figure 8

Supplementary Material 10: Supplementary Figure 9

Supplementary Material 11: Supplementary Figure 10

Supplementary Material 12: Supplementary Figure 11

Supplementary Material 13: Supplementary Figure 12

Supplementary Material 14: Supplementary Table 1

Supplementary Material 15: Supplementary Table 2

Supplementary Material 16: Supplementary Table 3

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Author contributions

ZYZ, DCY, and RJ contributed equally to this work as co-first authors. ZYZ, DCY, and RJ : Methodology, Data Curation, Formal Analysis, Visualization, Writing - Original Draft; NL and WX: Software, Formal Analysis, Visualization, Writing - Original Draft; YNZ and JZ: Formal Analysis, Visualization, Writing - Original Draft; YQY: Data Collection, Visualization, Writing - Original Draft and Writing - Review & Editing; TWG and ZGL: Conceptualization, Supervision, Project Administration, Writing - Review & Editing. All authors reviewed the manuscript.

Data availability

The datasets used and analyzed in this study are available from the Surveillance, Epidemiology, and End Results (SEER) Program at. SEER data are available upon submission of data requests. For more information on data access, visit the SEER website.

Declaration

Ethical approval

This study did not involve human participants or animals, and therefore, no ethical approval was required. All data used in this study were obtained from publicly available sources, and no individual-level data were accessed or analyzed.

Disclaimer

The views expressed in this article are solely those of the authors and do not necessarily reflect the official policy or position of any affiliated institutions or funding agencies.

Competing interests

The authors declare no competing interests.

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