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EFFECT OF MEDIASTINAL RADIOTHERAPY ON 30-DAY MORTALITY AFTER CARDIAC SURGERY

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Late complications affecting the cardiovascular system depend on the extent of the capture of cardiac structures in the radiation field and the cumulative dose of exposure. They are characterized by polymorphism in clinical manifestations. **Objective:** to identify the predictors influencing in-hospital mortality (IHM) in order to optimize the treatment of patients with radiation-induced heart disease. **Materials and methods.** This is a single-patient cohort study that was retrospective from 2004 to 2018 and prospective from 2018. Death after 30 days following heart valve surgery (HVS) under artificial circulation was taken as the end point of the study. The study included 86 patients (mean age 59 ± 13 years, 81.4% female) who underwent HVS. They were split into 2 groups (extensive, tangential) depending on the cause of cancer. **Results.** In the postoperative period, the group with extensive irradiation had statistically significant differences in the need for prolonged ventilation, OR 5.17 (CI 95% 1.7–15.7), more frequent exudative pleurisy OR 3.4 (CI 95% 1.1–10.8), and acute renal failure OR 1.2 (CI 95% 1.05–1.37). Regardless of postoperative complications, the length of hospital stay did not differ statistically across the groups, with a median of 10.5 (CI 7.25:16.75) *vs.* 11 (CI 9:15.25) days, respectively. Overall IHM was 14 (16.27%) patients. Multiple organ failure (MOF) was the cause of death in 9 cases. Multivariate analysis revealed that extensive irradiation for lymphogranulomatosis increased IHM risk by 5.099 times, and an increase in the EuroSCORE II score by every "1" increased IHM risk by 1.19 times. **Conclusion.** Patients with post-radiation damage to heart valves and coronary arteries with a history of tangential irradiation can be successfully operated on. Extensive irradiation in anamnesis is associated with a high risk of heart failure and MOF in the early postoperative period.

Keywords: radiation therapy, cardiac surgery, in-hospital mortality.

INTRODUCTION

Radiation therapy (RT) is widely used in the treatment of chest tumors, but its late cardiovascular complications depend on the extent of cardiac exposure and the cumulative radiation dose. These complications exhibit polymorphic clinical manifestations, with their development following a time-dependent pattern [1–3].

The earliest manifestation of radiation-induced cardiac damage is often coronary heart disease, which can become as significant as cancer itself within the first five years post-RT [4]. In contrast, radiation-induced valvular disease emerges later and follows a linear-quadratic progression model [5, 6]. Over time, radiation-induced heart injury advances and frequently presents as a complex syndrome, involving multiple cardiac structures alongside extracardiac complications.

Objective: to identify the predictors influencing in-hospital mortality (IHM) in order to optimize the treatment of patients with radiation-induced heart disease.

MATERIAL AND METHODS

Place and time of study

The study included patients treated at the Department of Emergency Surgery for Acquired Heart Defects, Bakulev National Medical Research Center for Cardiovascular Surgery in Moscow (Department headed by Prof. R.M. Muratov from 2002 to 2023, and by D.A. Titov from 2023 to the present), and it covered the period from June 2004 to May 2023.

Study population

The main inclusion criteria for the study were a documented history of RT, a minimum interval of 9 years from RT to the development of cardiac pathology, presence of valvular disease requiring surgical intervention, and clinical group 3 status (complete cancer remission) at the time of hospitalization for valvular surgery. Based on these criteria, the study included 86 patients who had previously undergone RT for breast cancer (tangential field) or Hodgkin's lymphoma (extensive field exposure).

Study Design

This single-cohort study was conducted retrospectively from 2004 to 2018 and prospectively from 2018 onward. The primary objective was to identify predictors of IHM in patients with radiation-induced cardiac lesions.

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The study endpoint was mortality within 30 days following cardiopulmonary bypass surgery for radiation-induced valvular disease.

Methods

All patients underwent clinical, laboratory, and instrumental examinations following standard cardiac surgical care protocols. The diagnostic criteria for stenosis and regurgitation were based on the 2021 guidelines of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) for managing valvular heart disease [7].

To assess mitral stenosis severity, echocardiographic evaluation included leaflet mobility, leaflet thickness, degree of subvalvular structure involvement, and annulus fibrosus calcification. Each parameter was scored from 1 to 4, with a maximum Wilkins score of 16 [8]. For patients with echocardiographic signs of mitral annular calcification, the severity was further evaluated using Rajesh Movva et al.'s criteria [9], with annulus fibrosus scoring and summation.

Coronary angiography was performed following the ESC/EACTS guidelines for myocardial revascularization [10]. For patients with extensive radiation exposure, diagnostic coronary angiography was conducted more broadly in the presence of clinical signs of coronary heart disease. To objectively assess the complexity of coronary artery lesions, the study used the SYNTAX Score (Synergy Between PCI With Taxus and Cardiac Surgery), a widely accepted anatomic classification system [11].

A chest CT scan was performed to assess the severity of calcification in cardiac structures and the presence of pneumofibrosis. Calcium deposits in the aortic valve, ascending aorta, and coronary arteries were measured using the Agatston method (1990) [12]. For Agatston score calculation, a 130 HU attenuation threshold was applied (130–199 corresponds to 1 point, 200–299 to 2 points, 300–399 to 3 points, 400 and above to 4 points). Each calcified area was assigned a score based on its attenuation value, then multiplied by the lesion area, with all values summed. The final total calcium score was calculated for the mitral annulus fibrosus, coronary arteries, and ascending aorta.

Pneumofibrosis was assessed using a semi-quantitative method, modifying the radiologic criteria for pneumofibrosis on a 0–3 scale for each lung lobe, where 0 = absent, 1 = linear streaks, 2 = moderate fibrosis, and 3 = severe fibrosis with bronchiectasis. The total pneumofibrosis score was obtained by summing the scores across all lung lobes [13].

For risk stratification based on the nature of surgery, the following logistic scoring systems were used to estimate 30-day mortality: EuroSCORE, EuroSCORE II, and STS PROM.

Statistical analysis

Normality of distribution was tested using the Kolmogorov–Smirnov test. Quantitative variables with normal distribution were processed using descriptive statistics, calculating mean ± standard deviation. On the contrary, variables with other type of distribution were evaluated by calculating the median and interquartile range (1st and 3rd quartiles). Qualitative variables were presented as absolute frequencies and percentages. When comparing groups with normal distribution, the data were analyzed using a parametric method (Student's t-test for independent samples), the rest of the data were analyzed using a non-parametric method (Mann–Whitney U test). A binary logistic regression model was used to identify IHM predictors (outcome: dead/alive). Previous preoperative RT, clinical and instrumental data were used as independent variables. A significance level of 0.05 was adopted for all statistical results.

Clinical material

The mean age of patients included in the study was 58.85 ± 12.71 years. The most widely represented age group were old patients from 60 to 74 years old; they made up 42 (48.84%) patients. Middle-aged patients (45–59 years old) were 15 in number (17.44%), while young patients (18–44 years old) were 23 (26.74%). The smallest group was the very old group according to the WHO classification (75–90 years), represented by 6 (6.98%) patients. Females prevailed over males, accounting for 70 (81.4%) patients. According to the etiology of the oncological disease, the patients were distributed as follows: Hodgkin's lymphoma (HL), 41 (46.67%) patients, and breast cancer (BC), 45 (53.33%) (Fig. 1).

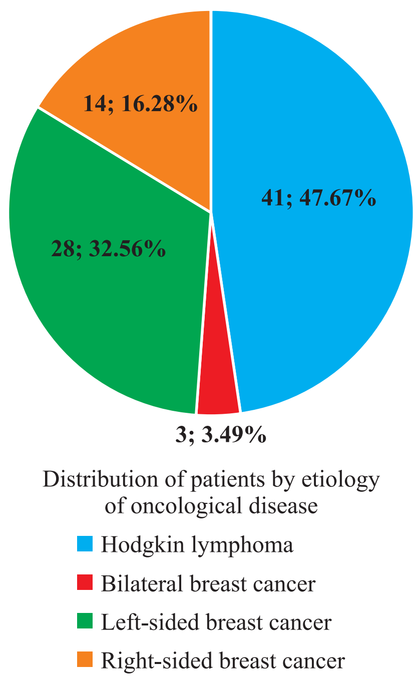

Fig. 1. Structure of oncological diseases

To evaluate demographic indicators, risk factors of cardiovascular diseases, comorbid pathology, combined diseases reflecting the severity of cardiovascular conditions and symptoms of circulatory failure and functional status depending on tumor type and direction of ionizing radiation in relation to the mediastinum, patients were divided into two conditional groups: extensive irradiation and tangential irradiation (Table 1).

RESULTS

Analysis of preoperative data revealed significant differences between the groups. The extensive irradiation group was notably younger. While the absolute values of coronary artery lesions were comparable, the number of combined lesions was significantly higher in this group. Additionally, coronary artery lesions in the extensive irradiation group were predominantly proximal.

Pearson's correlation analysis showed a significant inverse relationship between the year of RT and the time of cardiac pathology occurrence ($r = –0.897$, $p < 0.001$).

As shown in Table 2, hemodynamic parameters did not differ significantly. Most patients had aortic stenosis, with an average peak gradient of 80 ± 28 mmHg. The primary differences between the groups were in the morphofunctional parameters of the left ventricle. Indexed myocardial mass was significantly lower in the extensive irradiation group compared to the tangentially irradiated group (122 *vs.* 156 g/m^2, respectively). Additionally, a significantly higher proportion of patients in the extensive irradiation group had concentric hypertrophy (84.1% *vs.* 46.5%, $p < 0.001$). This phenomenon, known as 'immobilizing interstitial myocardial fibrosis,' is characterized by disruption of the endomysium and perimysium structure, leading to gradual mechanical compression and immobilization of the myocardium. Analysis of the mean fiber shortening fraction revealed a slight decrease in the tangential irradiation group, while the fraction remained preserved in the extensive irradiation group, possibly due to the high proportion of patients with arterial hypertension.

An integrated assessment of global longitudinal left ventricular (LV) strain parameters showed a significant decrease in the extensive irradiation cohort (11.1 ± 9%) and a moderate decrease in the tangential irradiation group (14.5 ± 3.2%). Despite volume overload in patients with mitral and aortic regurgitation, the proportion of those with eccentric hypertrophy remained low – 13.6% in the tangential irradiation group and 18.2% in the extensive irradiation group. These findings suggest that the observed changes can be interpreted in the context

Table 1

Clinical characteristics of patients

	Tangential (n = 45)	Extensive (n = 41)	General (n = 86)	P value
Age (years)	67 ± 7	49 ± 11	59 ± 13	**0.000**
BMI (kg/m^2)	29 ± 5.06	26.33 ± 4.56	27.8 ± 5	**0.07**
BSA (m^2)	1.87 ± 0.15	1.87 ± 0.22	1.87 ± 0.19	0.910
Interval between RT and surgical treatment of cardiac pathology (years)	23 ± 9	27 ± 9	25 ± 9	**0.044**
Age at the time of RT (years)	44.67 ± 9.29	22.37 ± 9.8	34.03 ± 14.63	**0.000**
Female	45 (100)	26 (60.9)	70 (81.4)	**0.000**
Combination chemotherapy, n (%)	27 (61.4)	36 (87.8)	63 (74.1)	**0.005**
NYHA functional class III and IV, n (%)	44 (53)	39 (47)	82 (95.34)	0.503
Pacemaker, n (%)	1 (25)	3 (75)	4 (4.6)	0.262
Arterial hypertension, n (%)	37 (62)	23 (38)	60	**0.08**
Atrial fibrillation, n (%)	6 (60)	4 (40)	10 (11.83)	0.605
CHD, n (%)	5 (26)	14 (74)	19 (22.09)	**0.010**
Diabetes mellitus, n (%)	13 (93)	1 (7)	14 (16.27)	**0.001**
COPD FEV_1 <50–80% FEV_1 <49–39%	11 2 36.6 40	19 3 63.4 60	30 5 34.88 5.8	**0.006**
SYNTAX Score	12 [8–16]	10 [3–16.5]	10.5 [4.7–16.2]	0.218
EuroSCORE I	6.35 [3.5–8.4]	3.89 [2.1–6.9]	4.9 [3.2–7.8]	**0.008**
EuroSCORE II	2.3 [1.6–4.9]	2.4 [1.5–4.4]	2.4 [1.6–4.7]	0.619
STS PROM	4.9 [3.4–6.2]	4.2 [1.9–6.8]	4.7 [2.5–6.9]	0.308
Creatinine clearance (CKD-EPI)	67 [54–78]	82 [66–104]	72 [57–89]	**0.001**

Note: BMI, body mass index; BSA, body surface area; RT, radiation therapy; NYHA, New York Heart Association; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second; SYNTAX Score, Synergy Between PCI With TAXUS and Cardiac Surgery Systematic Coronary Risk Evaluation; EuroSCORE I and EuroSCORE II, European System for Cardiac Operative Risk Evaluation; STS, Society of Thoracic Surgeons.

of myocardial fibrosis resulting from radiation exposure to the LV myocardium.

Echocardiographic assessment (Table 2) revealed a high incidence of mitral annular calcification in patients who RT for breast cancer. However, a semiquantitative analysis of calcification using Movva's criteria showed no significant differences between the groups.

While calcium deposition in cardiac structures was prevalent, there was no statistically significant variation between groups. Notably, extensive irradiation resulted in significant lung tissue exposure, leading to widespread pulmonary parenchymal fibrosis, which was markedly more severe in the extensive irradiation group (Table 2).

All patients underwent surgery with artificial circulation (Table 3). Although median cardiopulmonary bypass time differed between groups – 137 minutes (105–205) in the tangential group *vs.* 177 minutes (130–220) in the extensive group (p = 0.084) – the difference was not statistically significant. However, aortic clamping time was significantly longer in the extensive irradiation group (103 minutes [77–124] *vs.* 78 minutes [63–109], p < 0.018), likely due to the greater surgical volume. In most cases, the procedure was limited to a single-valve intervention, with aortic valve replacement performed in 51.7% of patients.

Due to post-RT skin changes preventing median sternotomy (Fig. 2), alternative surgical access was used in 20.98% of cases (n = 18), including J-shaped ministernotomy along the 4th intercostal space and, in one case, bipleural access.

Prolonged ventilation (PV) was required in 22 patients (25.58%), most commonly due to heart failure, which developed in 17 patients. Intra-aortic balloon counterpulsation was used in 7 patients, while extracorporeal membrane oxygenation (ECMO) was required in 4 cases. Acute renal failure developed in 5 patients (Fig. 3).

In the postoperative period, there were statistically significant differences in the need for PV (OR 5.17, CI 95% 1.7–15.7), more frequent exudative pleurisy (OR 3.4, CI 95% 1.1–10.8), and acute renal failure (OR 1.2, CI 95% 1.05–1.37) in the extensive radiation group. Re-

Table 2

Findings from instrumental diagnostic methods

	Tangential	Extensive	P value
Electrocardiographic parameters			
Preoperative HR (beats/min)	78.5 ± 13.4	84.39 ± 11.1	**0.033**
QT interval (sec)	0.397 ± 0.05	0.404 ± 0.05	0.547
QRS (sec)	0.1 [0.09–0.12]	0.108 [0.008–0.120]	0.336
Echocardiographic findings			
Left atrium, cm	5.1 ± 1	4.2 ± 0.809	0.118
LV end-diastolic volume (cm)	122 ± 35.1	127 ± 41.4	0.522
LV ejection fraction (%)	64 ± 10.3	62 ± 11.5	0.425
LV fractional shortening (%)	36 ± 8.05	34 ± 8.03	0.473
LV relative wall thickness	0.55 ± 0.13	0.47 ± 0.2	**0.016**
Mean circumferential fiber shortening fraction, %	12.5 ± 3.16	14.29 ± 3.1	**0.019**
Indexed myocardial mass, gr/	156 ± 67.1	122 ± 64.2	**0.006**
Mitral stenosis (n)	9	10	0.374
Peak diastolic gradient across MV, mmHg.	10 [7.5–13]	11 [9.7–13.5]	0.787
Annular calcification (n)	29	12	**0.024**
Calcification total score	7.38 [6.31–8.47]	6.7 [5.15–8.39]	0.802
Wilkins score	8.9 [7–10.7]	8.37 [7–9.7]	0.454
MV regurgitation > grade 2 (n)	13	22	**0.020**
Aortic stenosis >40 mmHg (n)	36	27	0.716
Aortic valve annulus size, mm	21.91 ± 2.44	21.7 ± 2.08	0.695
Aortic valve peak gradient, mmHg.	83 [73–93]	75 [65–85]	0.266
AV regurgitation > grade 2 (n)	8	8	0.916
LV systolic pressure, mmHg	38 ± 23	46 ± 17.2	0.189
Computer tomography			
Coronary artery calcification	681 [204–1158]	857 [442–1273]	0.334
Ascending aorta calcification	3018 [1649–4387]	2136 [1113–3159]	0.785
Aortic valve calcification	3945 [2227–5663]	2802 [1473–4132]	0.895
Mitral annular calcification	3872 [1596–6148]	2974 [881–5067]	0.9
Pulmonary fibrosis level	3.35 [2.45–4.25]	7.15 [5.9–8.41]	**0.0001**

Note: HR, heart rate; LV, left ventricular; MV, mitral valve; AV, aortic valve.

gardless of postoperative complications, the length of hospital stay was not statistically different between the groups, with a median of 10.5 (CI 7.25:16.75) *vs.* 11 (CI 9:15.25) days, respectively.

Overall, IHM was 16.27% (n = 14). Multiple organ dysfunction syndrome (MODS) was the leading cause of death in 9 cases. Among these, MODS resulted from acute cerebrovascular insufficiency in one case, respiratory failure in two cases, and acute heart failure in four cases during the postperfusion period. In these four cases, ECMO was required due to the ineffectiveness of intra-aortic balloon pump (IABP) in stabilizing hemodynamics. In two additional cases, IABP was initiated in the intensive care unit due to worsening heart failure.

In five cases, the immediate cause of death was acute heart failure. In two patients, heart failure resulted from ventricular fibrillation – one occurring on day 3 post-aortic prosthesis and mammary-coronary artery bypass of the anterior interventricular artery, and the other on day 9 after aortic valve replacement and coronary artery bypass grafting (CABG) in a patient with multivessel coronary artery disease, poor peripheral circulation, and aortic stenosis. Additionally, one case involved iatrogenic injury to the left coronary artery trunk due to massive arterial

Table 3

Scope of surgical intervention

	Tangential	Extensive	Σ
Single-valve intervention (n = 47)			
AV replacement	30 (66.7%)	14 (34.14%)	44
MV repair	1 (2.2%)	0	1
MV replacement	0	2 (4.9%)	2
Two-valve intervention (n = 26)			
MV and TV repair	1 (2.2%)	0	1
AV replacement and TV repair	1 (2.2%)	0	1
AV and MV replacement	3 (6.7%)	8 (19.5%)	11
MV and TV replacement	1 (2.2%)	0	1
AV replacement and MV repair	2 (4.4%)	3 (7.3%)	5
MV replacement and TV repair	1 (2.2%)	6 (14.6%)	7
Three-valve intervention (n = 13)			
AV, MV and TV replacement	0	1 (2.2%)	1
AV and MV replacement, and TV repair	4 (8.9%)	5 (12.2%)	9
AV replacement and atrioventricular valve repair	1 (2.2%)	2 (4.9%)	3
Additional procedures			
Jatene ventriculoplasty	0	1	1
Myocardial revascularization	5	14	19
Annulus fibrosus decalcification with repair	3	2	5
AV annulus fibrosus boring	0	1	1
Reoperation	2	1	3
Pericardiectomy	0	2	2

Note: AV, aortic valve; MV, mitral valve; TV, tricuspid valve.

Fig. 2. Radiation injury to the chest skin

calcification. In one case, early prosthetic endocarditis developed on day 16 after two-valve replacement, necessitating repeat surgery. However, this was complicated by acute heart failure in the postperfusion period. Another case of acute heart failure occurred during cardiac recovery following aortic and mitral valve replacement, tricuspid valve repair, and CABG of the anterior interventricular artery. Intra-aortic balloon counterpulsation failed to stabilize hemodynamics, and ECMO could not be initiated due to a high risk of bleeding.

Pathological and morphological examinations were performed on 11 patients. Histological analysis of the heart revealed interstitial and perivascular spaces replaced by collagen fibers (Fig. 4). Qualitative assessment of the micropreparations showed that cardiomyocyte replacement by collagen fibers averaged 33.1 ± 5.6%. Among patients who underwent mantle irradiation, interstitial fibrosis measured 32 ± 3.09%, while in the tangential irradiation group, it was 37 ± 7%.

Table 4

Multivariate analysis results

	Beta regression coefficient	P value	OR	95% confidence interval for OR	
				Lower	Upper
Extensive RT	1.510	0.033	4.526	1.130	18.129
EuroScore II	0.170	0.016	1.185	1.032	1.361
Constant	–3.282	0.000	0.038		

Note: OR, odds ratio; RT, radiation therapy; EuroSCORE II, European System for Cardiac Operative Risk Evaluation II.

Multivariate analysis using the stepwise exclusion method identified a predictive model with two significant factors influencing IHM (Table 4). Extensive chest irradiation for lymphogranulomatosis increased the risk of IHM by 5.099 times, while each 1-point increase in the EuroSCORE II scale raised the risk by 1.19 times. This model demonstrated satisfactory predictive accuracy, with an AUC of 75% (CI: 63–87%) (Fig. 5).

DISCUSSION

Advances in anticancer therapy have significantly reduced mortality for certain types of cancer. However, in the long term, treatment-related side effects and subsequent development of cardiovascular complications remain critical concerns for early detection and management. To mitigate these risks, baseline risk assessment for cardiac toxicity (Class I, Level of Evidence B) is recommended before initiating cancer treatment.

Stratifying risk levels for late complications can help identify patients at higher risk for unfavorable cardiovascular outcomes. However, many quality-of-care improvements, including guideline recommendations, were not introduced until the early 21st century. As a result, the ESC guidelines on cardio-oncology – developed in collaboration with the European Hematology Association (EHA), the European Society for Radiotherapy and Oncology (ESTRO), and the International Cardio-Oncology Society (ICOS) – were only published on August 26, 2022.

Treatment standards for this patient population have not yet been established, as no randomized trials exist

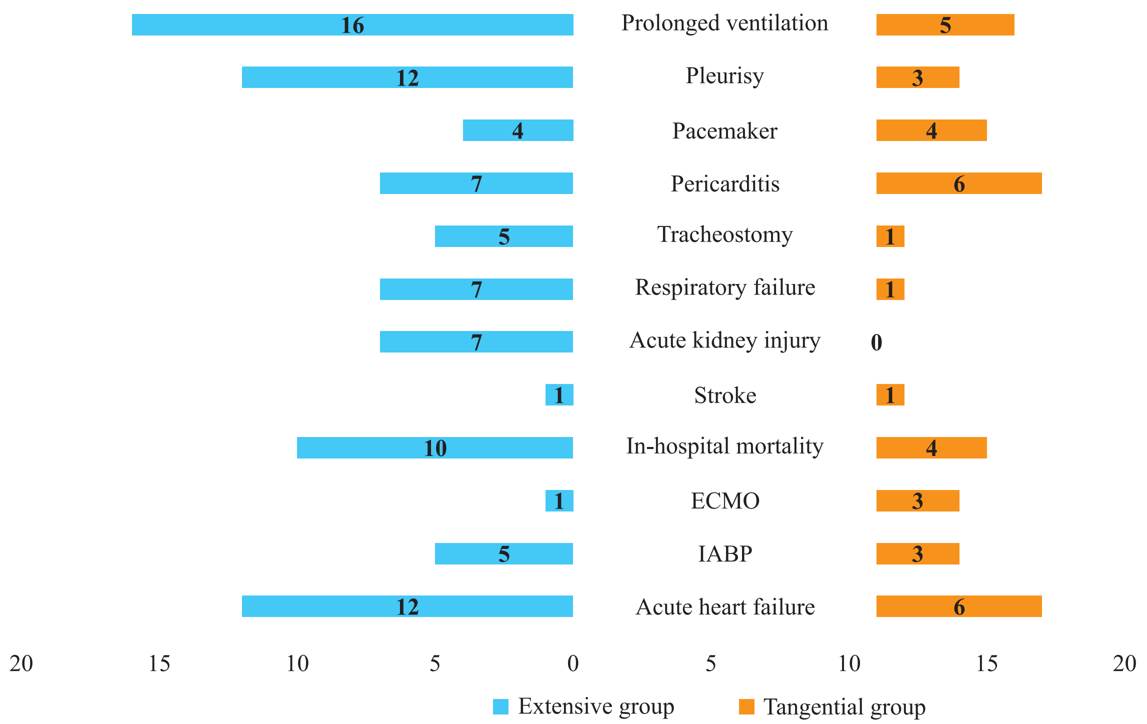

Fig. 3. Postoperative complications and in-hospital mortality. ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon counterpulsation

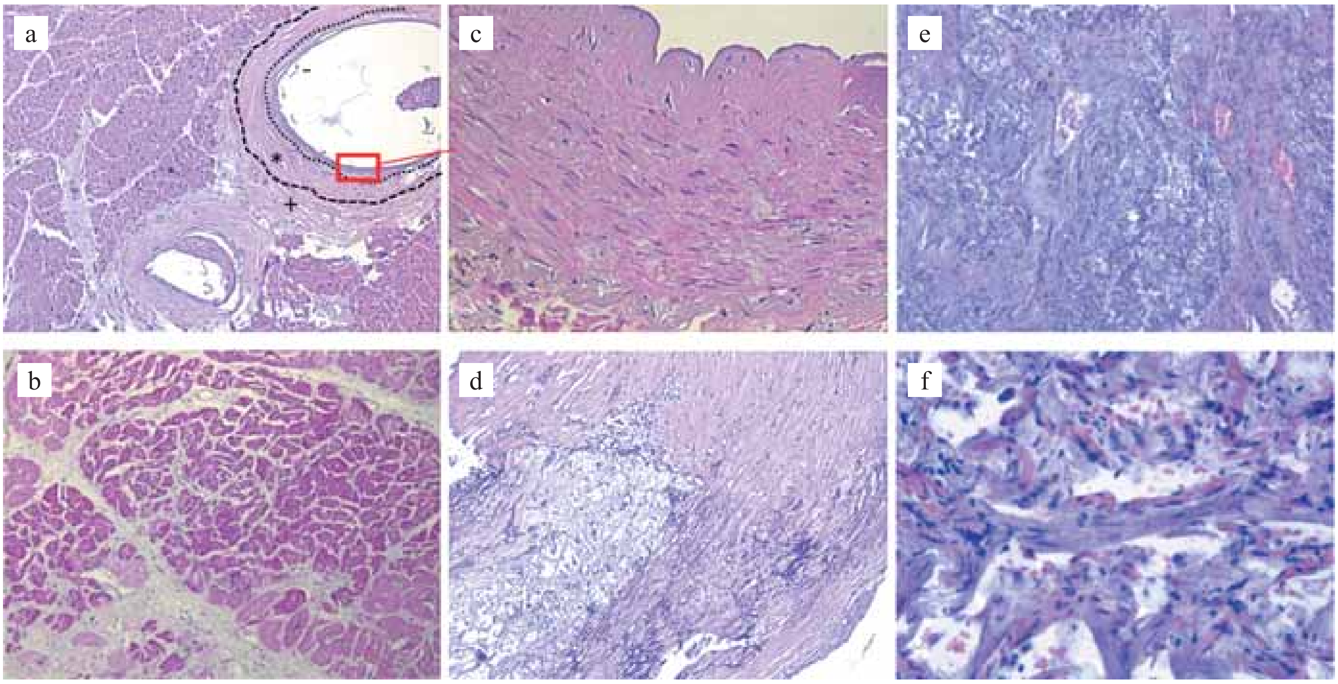

Fig. 4. Image 1 a, sclerosis and hyalinosis of all layers of intramural coronary arteries; +, adventitia, *, media, intima lens 10, eyepiece 10; b, left ventricular myocardial fibrosis. Myocardial fibrosis of the perivascular and interstitial space 42%. lens 20, eyepiece 10; c, diffuse thickening and fibrosis of the vessel intima lens 40, eyepiece 10; d, coronary artery wall calcification lens 20, eyepiece 10; e and f, pulmonary fibrosis

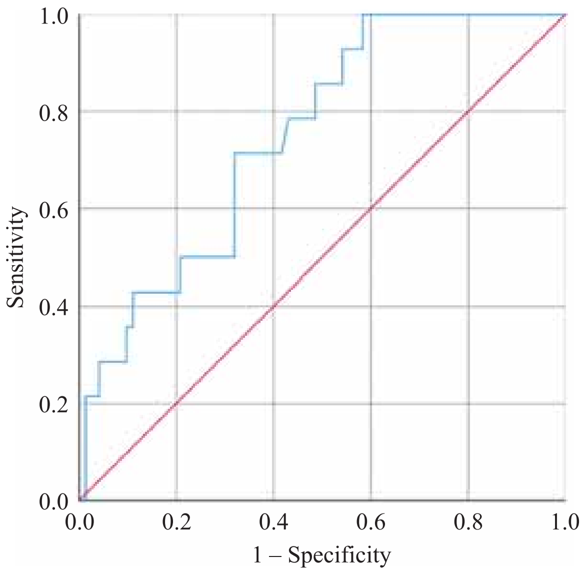

Fig. 5. ROC curve of the predictive model for the development of in-hospital mortality

due to the limited number of cases (competing secondary malignancies) and the unclear effects of prior treatments. Therefore, a multidisciplinary team approach is recommended to evaluate and determine surgical treatment options (Class I, Level of Evidence C).

The treatment principles for cardiac pathology in patients with prior radiotherapy (RT) generally align with conventional methods. However, the correction of valvular disease due to radiation exposure presents unique challenges. The 2017 ESC/EACTS guidelines provide limited guidance on RT-related valvular dysfunction, primarily recommending against conventional surgical treatment for aortic stenosis (Class I) in favor of transcatheter aortic valve replacement (TAVR), based on the heart team's discretion. The latest guidelines do not offer clear recommendations regarding RT-related valvular disease. However, the 2022 ESC cardio-oncology guidelines suggest that for patients at intermediate risk of complications, an alternative to TAVR (Class IIa, Level B) may be considered if severe aortic stenosis has resolved following radiotherapy [14].

Correlation analysis revealed an inverse relationship ($r = –0.897$, $p < 0.001$) between the year of RT and the interval before the development of cardiac pathology. However, this correlation is purely statistical and not a direct causal link to modern RT techniques. Instead, it reflects multiple contributing factors, particularly improved post-cancer therapy surveillance in high-risk survivors. For patients who underwent high-risk cancer therapy in childhood, echocardiographic screening is recommended every two years (Class IIa, Level B). In adults, annual risk stratification (class I, level B) is advised, with echocardiography at 1, 3, and 5 years after treatment (Class IIa, Level C).

With growing attention to cancer treatment-related complications, current guidelines emphasize risk stratification for late effects. In our study, we specifically analyzed a cohort with extensive irradiation. The evidence linking RT to heart failure is dose-dependent and follows a linear model for late complication development. A multicenter, retrospective case-control study demonstrated a high risk of heart failure in individuals exposed to high mean doses of left ventricular irradiation [15].

An EBCTCG study examined estimated cardiac radiation doses and their association with adverse cardiovascular events in 30,000 women over a 20-year follow-up. The analysis revealed a 3% increase in the risk of death from heart disease per Gy of average cardiac dose [16].

Additionally, Brown et al. compared extensive and tangential exposure groups, demonstrating that patients with tangential or minimal exposure had a lower risk of death compared to those with extensive irradiation (OR 0.6, 95% CI: 0.35–1.02, $p = 0.060$) [17].

Our meta-analysis demonstrated a 4.98-fold (95% CI 1.86–13.12; $p < 0.001$) increase in IHM risk in patients with a history of RT compared to a control group without RT [18].

The study also found that the extensive irradiation group was significantly younger, aligning with the findings of Chang et al., where the mean age in the tangential and extensive groups was 72 ± 8.8 *vs.* 51 ± 13 years, respectively ($p < 0.001$) [19]. Despite their younger age, patients in the extensive irradiation group experienced severe circulatory disorders due to the combined nature of the lesions and concomitant diseases.

Our data indirectly confirm that high-dose irradiation induces significant changes in all cardiac structures and is a key factor in the development of in-hospital mortality (IHM). In our study, IHM was 16.4%, whereas Ejifor reported rates of 3.8% for primary interventions and 17.4% for repeat procedures.

A potential explanation for this elevated IHM could be the extensive radiation exposure, leading to a high cumulative left ventricular radiation dose. However, these findings should be interpreted with caution. One major limitation is that the exact radiation dose to mediastinal structures was only available for a subset of patients due to the long history of prior radiotherapy.

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Secondly, during the treatment of breast cancer in the 1970s–1980s, RT targeting the internal mammary lymph node chain was commonly used to improve tumor control in internal quadrant lesions. Indirect signs of such irradiation, such as skin manifestations, can be observed in Fig. 2. This historical treatment approach likely explains the absence of significant differences in calcification of cardiac and ascending aortic structures. However, our findings highlight the critical role of myocardial interstitial fibrosis as a key predictor of IHM.

CONCLUSION

The degree of calcification in cardiac structures, the presence of pulmonary fibrosis, and the extent of cardiac surgery were not significant factors influencing IHM. Patients with post-radiation damage to heart valves and coronary arteries following tangential irradiation can successfully undergo surgery with artificial circulation. However, a history of extensive irradiation is associated with a high risk of cardiac and multiple organ failure in the early postoperative period. To reduce IHM, a more comprehensive assessment of both cardiac and non-cardiac complications from prior RT is essential.

The authors declare no conflict of interest.

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