



Original Article

Two-dimensional speckle tracking echocardiography in evaluating radiation-induced heart damage

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ARTICLE INFO

Keywords:

Radiotherapy

SBRT

Cardiotoxicity

Radiation-induced heart damage

Global longitudinal strain

ABSTRACT

Objective: Radiation-induced heart damage (RIHD) in malignant tumor patients with thoracic radiotherapy has been well documented. However, there is no study on the cardiac toxicity of stereotactic body radiotherapy (SBRT) based on two-dimensional speckle tracking echocardiography (2D STE).

Methods: In a prospective cohort trial, 48 patients with malignant tumor (including patients with lung cancer, pulmonary metastases and other tumor) were assigned to receive thoracic SBRT. Circulating biomarkers, electrocardiogram (ECG), echocardiography, and 2D STE were performed prior to and within two months after thoracic radiotherapy. The primary outcome of the trial was a decrease in global longitudinal strain (GLS) $\geq 10\%$. The secondary outcomes were major adverse cardiovascular events (MACE). Analysis were conducted using paired sample t-test, Wilcoxon signed rank test and Chi square test.

Results: The morbidity of RIHD is 44% within 2 months after SBRT in malignant tumor patients. Compared with pre-RT, a significant decrease in GLS was observed post-RT ($-17.98 \pm 3.54\%$ vs. $-16.92 \pm 3.41\%$; $P = 0.008$), without any significant change in left ventricular ejection fraction (LVEF) (68.54 ± 6.06 vs. 69.63 ± 4.45 ; $P = 0.234$), left ventricular mass (LVM) ($P = 0.342$), ECG parameters, creatine kinase ($P = 0.074$), cardiac troponin T ($P = 0.829$) or N-terminal pro-B-type natriuretic peptide ($P = 0.453$) at during the post-RT period. There was no evidence that RIHD was correlated with age ($P = 1.000$), mean heart dose ($P = 0.602$), BED ($P = 0.234$), EQD2/2 ($P = 0.615$), V5 ($P = 0.506$), V10 ($P = 0.578$), V20 ($P = 0.670$) and V30 ($P = 0.741$). Subgroup analysis showed, there is still a significant decline of GLS ($-18.30 \pm 3.79\%$ vs. $-17.11 \pm 3.58\%$; $P = 0.018$) in patients without anthracycline treatment. And the decrease of GLS ($-19.14 \pm 2.42\%$ vs. $-16.85 \pm 2.46\%$; $P = 0.004$) was more significantly post-RT in anthracycline treatment group. MACE were found in one patient over a period of two months after SBRT.

Conclusions: By using strain analysis subclinical cardiac dysfunction was found to be evident early after SBRT, despite unchanged conventional indices such as LVEF, ECG parameters or circulating biomarkers. And the decrease of GLS is still existed after the effect of anthracycline was removed.

Trial registration: ClinicalTrials.gov, registration number: NCT04443400.

Introduction

Radiotherapy is one of the most important treatment methods for malignant tumors. Although it plays an important role in the treatment of malignant tumors, radiotherapy can cause heart damage, which may partially offset the benefits of radiotherapy for cancer patients.¹

Though it is generally accepted that radiotherapy can cause heart damage, the global understanding of radiation-induced heart damage (RIHD) is still in its early phases.² At present, most studies on RIHD are based on retrospective studies of non-Chinese population. And they only focus on the long-term cardiac effects of radiotherapy, and pay little attention to the short-term cardiac damage after radiotherapy.³ Meanwhile, the long-term damage must be based on a series of structural and

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functional changes after radiotherapy.

Long before the onset of clinically cardiac events, subclinical cardiac changes may occur during the RT, at the completion of the RT, or weeks, months, or first year after the RT, that can be detected as functional dysfunction.⁴ Early detection of RIHD may have important clinical significance for cancer patients, especially young cancer patients. Furthermore, it may be essential for the prediction and protection of late RIHD.

Previous studies have shown that when the radiation reaches a specific dose, global longitudinal, circumferential, and radial strain as well as strain rate are substantially decreased, which can be detected by 2D STE before the decrease of left ventricular ejection fraction (LVEF) and the appearance of clinical symptoms.^{5,6}

Therefore, we conducted a prospective cohort study to evaluate the early changes of cardiac structure and function based on circulating biomarkers, electrocardiogram (ECG) parameters, echocardiography, and two-dimensional speckle tracking echocardiography (2D STE) in malignant tumor patients treated by stereotactic body radiation therapy (SBRT).

Methods

Trial oversight

This study was an investigator initiated, monocenter, unblinded trial that was conducted at our hospital. The authors assume responsibility for the accuracy and completeness of the data and analysis as well as for the fidelity of the trial. Major adverse cardiovascular events (MACE) was defined as unstable angina, new arrhythmia, acute myocardial infarction, heart failure, valvular heart disease, acute pericarditis, and cardiac death in this study.

Patients

Sixty-five consecutive patients with malignant tumor were prospectively screened, of whom 48 patients were recruited from April 2020 to

June 2021 (Figure 1). Inclusion criteria were malignant tumor patients at the age of 18–85 who were treated by transthoracic radiotherapy. Prior radiotherapy, acute coronary syndrome, heart failure (NYHA III-IV), arrhythmia requiring intervention, echocardiographic images that could not be satisfactorily obtained, or significant valvular heart disease (defined as more than mild valvular regurgitation or stenosis) were exclusion criteria. Written informed consent was obtained from all recruited patients. Informed consent was signed by all study participants. Our study was in accordance with all the ethical requirements and followed the reporting guideline for case series.

Radiotherapy

All patients were treated with SBRT. Before radiotherapy, the chest computed tomography (CT) examination will be carried out to locate the target area. According to the location of CT, the treatment target area is gross tumor volume (GTV) and planned target volume (PTV) is appropriately expanded on the basis of the former target. The treatment plan was made by multiplan 4.6 planning system. After the plan had been made, it was verified first, and then the stereotactic radiotherapy robot was used. According to the treatment plan, the cardiac minimum dose, mean dose, maximum dose, V5, V10, V20 and V30 were registered for each case. To evaluate the effect of radiotherapy dose on heart more accurately, we converted all maximum and mean cardiac doses to the biologically effective doses (BED), assuming an α/β ratio of 3 for the heart, with conversion to an equivalent dose in 2-Gy fractions (Eq. $D2/2$) using the linear quadratic model.^{7–9} The BED was calculated using the equation $nd[1+d/(\alpha/\beta)]$, the $EQD2/2$ was calculated from the dose–volume histograms as $nd[(d+\alpha/\beta)\div(2+\alpha/\beta)]$, n is a number of fractions, d is dose per fraction, and α/β was 3 Gy.¹⁰

Echocardiography and two-dimensional speckle tracking echocardiography

Echo-Doppler data were obtained using commercially available ultrasonography systems. LVEF was calculated by the modified Simpson or

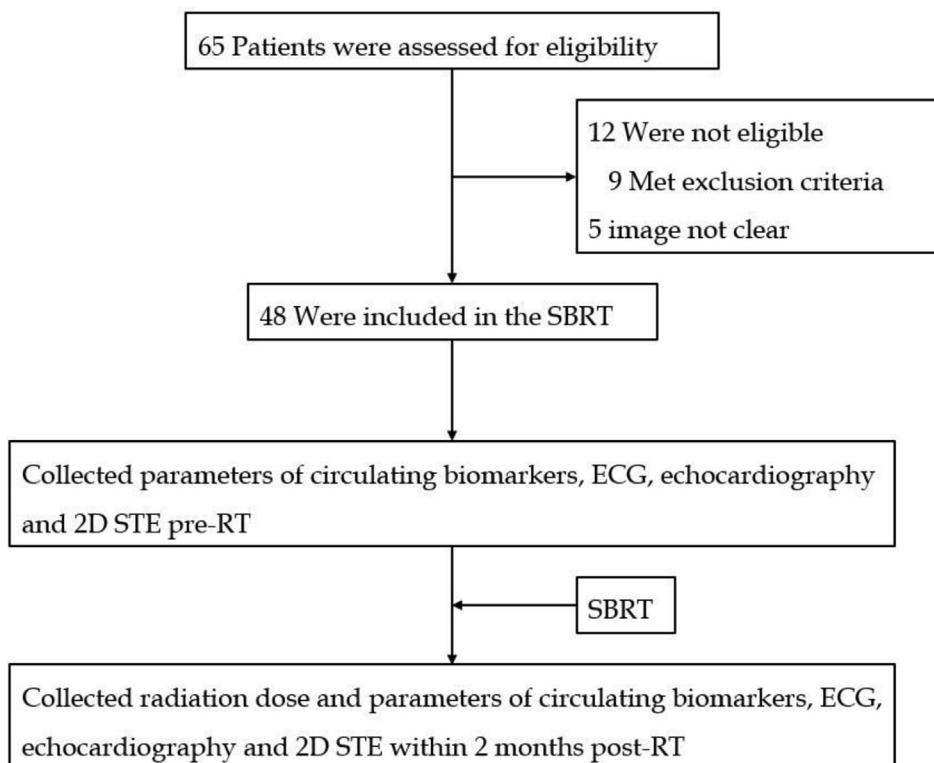


Figure 1. Enrollment, screening, and follow-up. Details regarding inclusion criteria and exclusion criteria, SBRT, and follow-up strategies are provided in the text. ECG, electrocardiogram; SBRT, stereotactic body radiotherapy; 2D STE, two-dimensional speckle tracking echocardiography; RT, radiotherapy.

the modified Quinones method. LV mass index was calculated by the Devereux formula and indexed for body surface area. Offline two-dimensional speckle-tracking strain imaging (2D-STI) analysis was performed from stored transthoracic echocardiography images (DICOM) using TomTec (TomTec Imaging Systems GmbH, Unterschleissheim, Germany). Frame rates were at least 30 per second in all patients. In order to assess the LV longitudinal strain by means of 2D-STI, standard 2D grayscale images of the LV were acquired from conventional, apical 2-, 3-, and 4-chamber views. Global longitudinal strain (GLS) was calculated as the peak strain value from the averaged strain curve generated from 16 segments. Subjects were excluded from the analysis if there were more than three segments judged as unsatisfactory.

Evaluation of cardiac structure and function

We evaluated the electrical activity of the heart by ECG, the cardiac structure (including pericardium, valve, atrioventricular diameter and wall thickness), systolic and diastolic function by echocardiography, the global longitudinal strain at baseline by two-dimensional speckle tracking echocardiography, and the presence of myocardial damage by cardiac damage markers [including creatine kinase (CK), CKMB, troponin T (cTnT), N-terminal pro-B-type natriuretic peptide (NT-proBNP)].

Follow-up and data analysis

Echocardiography, 2D STE, CK, CK-MB, cTnT, NT-proBNP, electrocardiogram (ECG), and hs-CRP were detected before and after radiotherapy. All the participants were followed within 2 months after their completion of thoracic radiotherapy (post-RT).

Continuous variables are presented as mean and standard deviation or median and interquartile range as appropriate, whereas categorical variables are presented as frequency and percent. Paired sample t-test was used to compare continuous variables conforming to normal distribution, Wilcoxon signed rank test was used to compare continuous variables not conforming to normal distribution. Chi square test was used to evaluate the risk factors of RIHD. Statistical analysis was performed using SPSS22.0 software. *P*-value < 0.05 will be considered significant.

Ethics considerations

The study was approved by the Ethics Committee of Peking University Third Hospital (IRB00006761-M2020074). The trial was conducted in compliance with the Declaration of Helsinki (amended at the 64th World Medical Association General Assembly, Fortaleza, Brazil, October 2013).

Results

From April 7, 2020 to June 20, 2021, a total of 48 patients were enrolled at our hospital. The baseline patient demographics and cardiovascular risk factors are presented in Table 1. Among all the enrolled patients, 29 (60.4%) were lung cancer, 17 (35.4%) were pulmonary metastases, and 2 (4.2%) were patients with other malignant tumors receiving transthoracic radiotherapy (one was cardiac metastase and the other was thoracic vertebrae tumor). 20 patients had a history of chemotherapy, of which 13 patients had been treated with anthracyclines. Considering the prevalence of cardiovascular risk factors, 25.0% of the patients had hypertension, 16.7% with diabetes, 16.7% with dyslipidaemia, 12.5% with ischaemic heart disease, 29.2% with a history of smoking, and 4.2% with a family history of ischaemic heart disease of early onset.

All patients received SBRT. The median prescribed dose was 40 Gy (range, 24–50 Gy) in a median of 3 fractions (range, 1–7). The average minimum, mean and maximum heart doses were 77.08 cGy

Table 1
Characteristics of the patients at baseline.

Parameter	n (%)
Age, years, median (range)	60.5 (18-82)
Male	25 (52.1)
Blood pressure (mmHg, mean ± SD)	
Systolic blood pressure	128.5 ± 12.9
Diastolic blood pressure	75.6 ± 10.0
Tumor classification	
Lung cancer	29 (60.4)
Pulmonary metastasis tumor	17 (35.4)
Non-lung tumor	2 (4.2)
Tumor localization	
Upper lobe of left lung	17 (35.4)
Lower lobe of left lung	7 (14.6)
Upper lobe of right lung	5 (10.4)
Middle lobe of right lung	2 (4.2)
Lower lobe of right lung	4 (8.3)
Multiple lobes	11 (22.9)
Right atrium	1 (2.1)
7th thoracic vertebra	1 (2.1)
Tumor stage	
I	9 (18.6)
II	2 (4.2)
III	2 (4.2)
IV	35 (72.9)
Tumor size (mm ³)	8909.00 (159.00, 538,068.00)
Risk factors of cardiovascular disease	
Hypertension	12 (25.0)
Diabetes	8 (16.7)
Dyslipidaemia	8 (16.7)
IHD	6 (12.5)
Smoking	14 (29.2)
Family history of IHD	2 (4.2)
Medication use	
Chemotherapy history	20 (41.7)
Anthracycline	13 (27.1)
Platinum	9 (18.8)
Cyclophosphamide	5 (10.4)
Paclitaxel	6 (12.5)
Beta-blockers	2 (4.2)
ACE-inhibitor/ARB	8 (16.7)
Statins	6 (12.5)

IHD, ischaemic heart disease; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker.

(1.69–322.18 cGy), 593.24 cGy (37.95–1457.90 cGy), and 2725.35 cGy (111.47–6121.08 cGy) respectively. Converted to EQD2/2, the median cardiac maximum EQD2/2 was 108.00 Gy_{2/2} (range, 40.00–198.00 Gy_{2/2}). 32 patients (66.7%) had a maximum EQD2/2 > 100 Gy, and 15 (31.3%) had a maximum EQD2/2 > 150 Gy. The median values of V5,

Table 2
Radiotherapy data.

Parameter	Median	Range
Prescription dose (Gy)	40	24-50
Fractionation	3	1-7
PTV (mm ³)	32,104.00	3931.00–37,0520.00
GTV (mm ³)	8909.00	159.00–538,068.00
Minimum heart dose (cGy)	59.45	1.69–322.18
MHD (cGy)	646.13	37.95–1457.90
Maximum heart dose (cGy)	2275.50	111.47–6121.08
V5 (%)	50.55	0–99.1
V10 (%)	17.35	0–75.4
V20 (%)	0.50	0–25.1
V30 (%)	0	0–19.7
BED (Gy)	180.00	67.00–330.00
EQD2/2 (Gy)	108.00	40.00–198.00

PTV, planned target volume; GTV, gross tumor volume; MHD, mean heart dose; V5,V10,V20,V30, percentage of volume receiving > 5, > 10, > 20, and > 30 Gy, respectively; BED, biologically effective doses; EQD2/2, equivalent dose in 2-Gy fractions.

V10, V20 and V30 were 50.55% (range, 0–99.1%), 17.35% (range, 0–75.4%), 0.5% (range, 0–25.1%) and 0 (range, 0–19.7%). 21 patients (44%) had a cardiac maximum dose > 30 Gy. Eight patients (17%) had a mean cardiac dose >10 Gy. The median cardiac BED was 180.00 Gy (range, 67.00–330.00 Gy) (Table 2).

Follow-up data for all outcomes were available through February 20, 2021. No patients were missing from the follow-up to the primary outcome.

During the follow-up period after radiotherapy, GLS of 44% (21/48) patients decreased ≥10% from baseline. And a significant decline in GLS from baseline was observed post-RT (−17.98 ± 3.54% vs. −16.92 ± 3.41%; *P* = 0.008). Among them, GLS of 32 patients decreased from baseline, two patient's GLS remained unchanged, and 14 patients' GLS improved compared with the pre-RT GLS. And, there was no significant difference in the parameters of circulating serum biomarkers (excluded CKMB), heart rate, left ventricular end systolic volume, left ventricular end diastolic volume, LVEF, Peak E, Peak A, E/A ratio, e', E/e' and LAP after SBRT (Table 3). In this study, acute pericarditis and acute heart failure occurred in one patient one month after SBRT. GLS decreased from -20.3% at baseline to -14.3% after two months of SBRT. A 29.6% drop of GLS appeared in this patient.

Subgroup analysis showed that, there is still a significant decline in GLS from baseline was observed after SBRT (−18.30% ± 3.79% vs. −17.11% ± 3.58%; *P* = 0.018) in patients without anthracycline treatment. And in anthracycline treatment group, the decrease of GLS (−19.14% ± 2.42% vs. −16.85% ± 2.46%; *P* = 0.004) was more significantly post-RT.

In this trial, we found that RIHD is not correlated with age (*P* = 0.575), BED (*P* = 0.575), EQD2/2 (*P* = 0.537), and anthracycline therapy history (*P* = 0.390) (Table 4).

The GLS of a 72-year old female who had lung cancer was −14.27% before SBRT. Then she received SBRT of which the prescribed dose was 45 Gy in 3 fractions. The average cardiac minimum dose, mean dose, maximum dose, BED, and EQD2/2 were 0.27 Gy, 2.21 Gy, 9.20 Gy, 270 Gy, and 162 Gy, respectively. Her GLS dropped 30.2% to −10.61% after the SBRT (Figure 2).

Table 3
Parameters of circulating biomarkers, echocardiography, and 2D STE.

	Mean ± SD (baseline)	Mean ± SD (post RT)	<i>P</i>
Circulating biomarkers			
CK	88.74 ± 60.39	75.00 ± 39.59	0.074
CK-MB	10.24 ± 8.07	8.00 ± 3.94	0.029
cTnT	0.012 ± 0.009	0.011 ± 0.008	0.829
NT-proBNP	153.87 ± 272.57	192.95 ± 387.00	0.453
Hs-CRP	14.046 ± 23.873	8.211 ± 17.173	0.107
ECG			
Heart rate	76.49 ± 17.99	81.19 ± 15.94	0.085
P-R intervals	149.12 ± 35.37	154.34 ± 17.95	0.323
QRS wave	87.12 ± 10.53	87.94 ± 19.56	0.249
QTC	384.96 ± 75.13	412.61 ± 29.77	0.756
Parameters of ECHO and 2D STE			
LVESV	46.17 ± 4.15	45.63 ± 3.86	0.348
LVEDV	28.23 ± 3.23	27.59 ± 2.72	0.166
LVEF	68.54 ± 6.06	69.63 ± 4.45	0.234
LVM	113.03 ± 29.38	108.80 ± 26.32	0.342
Peak E	0.71 ± 0.18	0.71 ± 0.17	0.834
Peak A	0.78 ± 0.18	0.80 ± 0.23	0.480
E/A ratio	0.96 ± 0.32	0.97 ± 0.41	0.815
e'	11.16 ± 2.92	10.82 ± 3.08	0.353
E/e'	6.31 ± 2.14	6.09 ± 1.54	0.519
LAP	9.23 ± 2.73	9.00 ± 1.91	0.610
GLS	−17.98 ± 3.54	−16.92 ± 3.41	0.008

CK, creatine kinase; CK-MB, creatine kinase isoenzyme; cTnT, cardiac troponin T; NT-proBNP, N-terminal pro-B-type natriuretic peptide; hs-CRP, hypersensitive C-reactive protein; LVEF, left ventricular ejection fraction; LVM, left ventricular mass; GLS, global longitudinal strain; 2D STE, two-dimensional speckle tracking echocardiography.

Table 4
Relationship between RIHD and dose, age and beta-blockers.

	RIHD, n (%)	Non-RIHD n (%)	<i>P</i>
Age, years			
< 50	7 (50.0)	7 (50.0)	0.575
≥ 50	14 (41.2)	20 (58.8)	
BED (Gy)			
< 150	7 (50.0)	7 (50.0)	0.575
> 150	14 (41.2)	20 (58.8)	
EQD2/2 (Gy)			
< 100	8 (50.0)	8 (50.0)	0.537
> 100	13 (40.6)	19 (59.4)	
Anthracyclines			
Yes	7 (53.8)	6 (46.2)	0.390
No	14 (40.0)	21(60.0)	

RIHD, radiation-induced heart damage; BED, biologically effective doses; EQD2/2, equivalent dose in 2-Gy fractions.

Discussion

In this single-center study of malignant tumor patients treated by radiotherapy, we used echocardiography, 2D STE, circulating biomarkers and ECG to evaluate early subclinical heart changes induced by radiation. And we have demonstrated two important findings with respect to two-month cardiotoxicity following SBRT in malignant tumor patients. Firstly, nearly half of the patients had RIHD within two months after SBRT. Secondly, GLS decreased significantly after SBRT, however, no significant changes were found in circulating serum biomarkers (excluded CKMB), ECG, LVEF, LVM, peak E, peak A, E/A ratio, e', E/e', and LAP compared with their pre-RT levels. Subgroup analysis showed that the change still existed after the effect of anthracycline was removed.

We reported that RIHD appeared in about half of the patients within two months after SBRT for the first time. In accordance with the existing studies, we found the changes of GLS appeared earlier than that of LVEF, CK, cTnT, NT-proBNP, and ECG parameters.

GLS is a reliable tool of early detection for radiation-induced heart damage. Myocardial strain analysis uses the principle of reflection and scattering when the sound beam meets the myocardial tissue interface. By continuously tracking the movement track of the acoustic spots in the myocardium, we can quantitatively analyze the myocardial movement displacement, velocity, strain, strain rate, and heart rotation angle. It has no angle dependence, and can accurately reflect the myocardial movement.³ It is an effective method to evaluate regional myocardial function.^{11,12} A 10% decrease of GLS can be used for the early detection of the subclinical heart damage.¹³

Radiation can cause RIHD in many ways, such as oxidative stress, mitochondrial damage, microvascular endothelial damage and atherosclerosis, leading to myocardial ischemia and energy metabolism disorders. Radiation can lead to mitochondrial dysfunction and affect the activity of mitochondrial electron transport chain complex, resulting in excessive production of reactive oxygen species (ROS) and cardiomyocyte apoptosis.¹⁴ Excessive production of ROS and other free radicals can mediate the epigenetic changes of fibroblasts through targeting DNA methylation, histone methylation and acetylation, thus inducing fibroblasts to differentiate into myofibroblasts.¹⁵ Studies have shown that after radiation exposure, the levels of inflammatory factors and pro-fibrotic factors [such as interleukin (IL)-1, IL-6, IL-8, platelet-derived growth factor, insulin-like growth factor and transforming growth factor-β (TGF-β), etc.] are increased to promote the formation of ROS and then lead to inflammatory reaction, in which TGF-β1 plays an important role in radiation-induced cardiac fibrosis.^{16–18} Radiation can cause the swelling and apoptosis of vascular endothelial cells, induce the secretion of inflammatory chemokines, and lead to the degradation of endothelial basement membrane.¹⁹ In animal experiments, the microvessel density of mouse heart tissue decreased significantly after

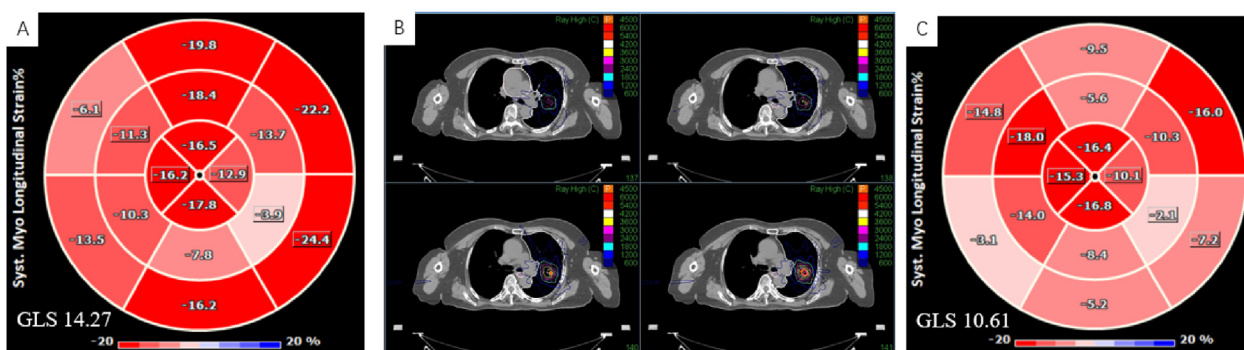


Figure 2. Strains analysis and SBRT data. A: Representation of regional myocardial damage in a lung cancer patient with 4-chamber, 2-chamber, and 3-chamber longitudinal strain curves and segmental (bull's eye) model of GLS pre-RT; B: Representation of SBRT plan; C: Representation of regional myocardial damage in the same patient with 4-chamber, 2-chamber, and 3-chamber longitudinal strain curves and segmental (bull's eye) model of GLS post-RT. RT, radiotherapy; SBRT, stereotactic body radiotherapy; GLS, global longitudinal strain.

irradiation.²⁰ It is suggested that radiation can cause vascular endothelial cell damage and myocardial fibrosis, eventually leading to the change of cardiac structure and cardiac dysfunction. In addition, radiation can also lead to the dysfunction of calcium regulation in endoplasmic reticulum, affecting cardiac systolic and diastolic function.²¹ Studies have shown that the level of atherosclerosis in the anterior descending branch of patients with left breast cancer after radiotherapy is significantly higher than that of other blood vessels, suggesting that radiation can promote the occurrence of atherosclerosis, which may be related to microvascular endothelial damage caused by radiation.²²

Myocardial damage and/or fibrosis induced by radiation may be the mechanism of GLS decrease. A prospective study, included 81 chemotherapy-naïve early-stage breast cancer patients, demonstrated the decline of GLS after radiation in the three-year follow-up examination.²³ This short-term decrease in GLS is perhaps related to long-term RIHD.

We found that there was statistical difference in CKMB levels before and after SBRT. CKMB level before SBRT was higher than that after SBRT. In some patients, CKMB was higher than the normal range, while cTnT was within the normal range. Therefore, we did not consider that the increase of CKMB was caused by myocardial damage. This may be related to the detection methods. For the determination of CKMB, the immunoinhibition method is utilized most commonly. However, the estimated CKMB activity may be influenced by the presence of creatine kinase isoenzymes in some conditions like cancer.²⁴ This abnormality could be explained by the unexpected appearance of CK-BB (brain type) or macro-CK, the complex composed of CKBB and immunoglobulin (type 1) or another creatine kinase isoenzymes derived from mitochondria (type 2).²⁵ Earlier case reports had described that false increase of CKMB, even higher than whole creatine kinase, was observed in the sera of patients with neoplasms but not myocardial infarction.^{24,26}

LVEF and circulating serum biomarkers may not change before the serious damage of cardiac structure.³ In the stage of subclinical heart damage, left ventricular structure will not change significantly, and serious myocardial cells damage may not occur. Studies have shown that troponin T is rarely abnormal in the early stage of most radiation-induced heart diseases.²⁷

Brain natriuretic peptide (BNP) is mainly synthesized and secreted by ventricular muscle cells. Its secretion is affected by ventricular wall tension. Nellesen et al. found elevated levels of BNP after radiotherapy, but the outcomes were not characterized as clinically significant.²⁸ However, D'Errico et al. clearly demonstrated increased levels of NT-proBNP in left-sided breast cancer patients within 5–22 months after radiotherapy.²⁹ Palumbo I et al. reported that BNP increased significantly ($P < 0.001$), particularly within 1–6 months after radiotherapy. It slightly decreased after 12 months.³⁰ However, we did not find the change of NT-proBNP after

radiation in this study. This may be affected by the type of tumor, the method of treatment, the dose received by the ventricle and other factors. Therefore, more large-scale studies are needed to evaluate the value of NT-proBNP in the early detection of radiation-induced heart damage.

In this study, we did not find the correlation between RIHD and age, radiation dose, and chemotherapy history before SBRT, which is different from previous research results.^{31–34} The small sample size, the location of radiotherapy, the left ventricular dose, the types of cancer, and the race may affect our conclusion in this study. More large-scale studies are needed to further clarify the possible risk factors of RIHD.

In the stage of subclinical cardiac damage, LVEF and serum markers may not change. This further highlights the advantages of GLS as an early detection index of radiation-induced heart damage.

As far as we know, this is the first prospective study from China to research the early stage of RIHD. In this study, the follow-up time frame after radiotherapy was controlled within two months, which reduced the impact of other unknown factors on the results effectively. All the patients were treated with SBRT in this study. Compared with traditional radiotherapy, SBRT has the advantages of high effective rate and less damage to non-tumor tissues. However, there is no report on cardiac damage after SBRT. Furthermore, this study explored the changes of short-term myocardial strain after radiotherapy, and go a step further in clarifying the cardiotoxicity of radiotherapy in the early stage.

Limitations

There are some limitations to this study. First, the sample size was small, which might represent a beta error. Second, as the follow-up time frame in this study was limited to two months, subclinical and clinical cardiac changes may not occur during this period in some participants. A more larger study over a longer follow up time period would be required to validate our current observations and to determine its impact on long-term adverse outcomes.

Conclusions

This study found that by using strain analysis subclinical cardiac dysfunction was found to be evident early after SBRT, despite unchanged conventional indices such as LVEF, ECG parameters, or circulating biomarkers. And the decrease of GLS is still existed after the effect of anthracycline was removed.

Declaration of competing interest

None declared.

Funding

This study was funded by Peking University Third Hospital (Grant No. BSYLXHG2020003).

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