Impact of long-axis function on cardiac surgical outcomes in patients with radiation-associated heart disease

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ABSTRACT

Background: Malignancy-associated thoracic radiation leads to radiation-associated cardiac disease (RACD) that often necessitates cardiac surgery. Myocardial dysfunction is common in patients with RACD. We sought to determine the predictive value of global left ventricular ejection fraction and long-axis function left ventricular global longitudinal strain (LV-GLS) in such patients.

Methods: We studied 163 patients (age, 63 ± 14 years; 74% women) who had RACD and underwent cardiac surgery (20% had reoperations) between 2000 and 2003. In addition to standard echocardiography, LV-GLS (%) was derived from the average of 18 segments in 3 apical views of the left ventricle, using velocity vector imaging. Standard clinical and demographic parameters were recorded. All-cause mortality was recorded.

Results: The mean duration between cardiac surgery and the last chest radiation was 18 ± 12 years. The median European System for Cardiac Operative Risk Evaluation (EuroSCORE) was 8, and 88 patients died over 6.6 ± 4 years. A total of 52% of patients had ≥II+ mitral regurgitation; 23% of patients had severe aortic stenosis; and 39% of patients had ≥II+ tricuspid regurgitation. The mean left ventricular ejection fraction was 54% ± 13%, and the mean LV-GLS was −12.9% ± 4%. In a Cox proportional survival analysis, lower LV-GLS was predictive of mortality in univariable analysis (hazard ratio, 1.07 (95% confidence interval, 1.01-1.14); P = .006); however, after adjustment for other variables, the association became nonsignificant. In patients with a EuroSCORE <median, abnormal LV-GLS (<−14.5%) was associated with significantly higher mortality (48%), compared with those with normal LV-GLS (32%).

Conclusions: In patients who have RACD and undergo cardiac surgery, LV-GLS does not sufficiently discriminate and is not independently predictive of long-term outcomes. However, in patients with a low EuroSCORE, abnormal LV-GLS was associated with higher mortality, compared with those with normal LV-GLS. (J Thorac Cardiovasc Surg 2015;149:1643-51)
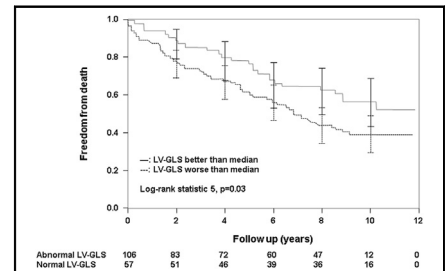
Kaplan-Meier survival curves of the entire study population, separated on the basis of preserved versus abnormal left ventricular global longitudinal strain (*LV-GLS*)

Central Message

In 163 patients with radiation-associated cardiac disease, lower left ventricular global longitudinal strain (LV-GLS) was predictive of mortality on univariable (HR, 1.07 [1.01-1.14]; P = .006) but not on multivariable analysis. In patients with low Euroscore, LV-GLS <−14.5% was associated with significantly higher mortality (48%) versus higher LV-GLS (32%).

Perspective

Radiation-associated cardiac disease (RACD) patients are a challenging group who have a heterogeneous presentation (coronary artery disease, valvular disease, cardiomyopathy or pericardial disease) often requiring complex cardiac surgeries. There is a high rate of mortality that is not entirely explained by progressive decline in global left ventricular (LV) function. Assessment of LV-global longitudinal strain (GLS), while being more sensitive at determining regional LV dysfunction, does not add independent incremental utility to determine long-term outcomes, in addition to Euroscore. However, patients with preserved LV ejection fraction but abnormal LV-GLS represent a higher risk subgroup in which assessment of LV mechanics might provide incremental utility. Similarly, lower risk patients with a low Euroscore but abnormal LV-GLS represent a higher risk subgroup in which assessment of LV mechanics might provide incremental utility. In RACD patients, a comprehensive cardiopulmonary evaluation is necessary before referring them for cardiac surgery. In patients that show high-risk features, alternate therapies like percutaneous coronary intervention and transcatheter valvular therapies should be considered.

Abbreviations and Acronyms

CABG	= coronary artery bypass grafting
CI	= confidence interval
EuroSCORE	= European System for Cardiac Operative Risk Evaluation
GLS	= global longitudinal strain
HR	= hazard ratio
LV	= left ventricular
LVEF	= left ventricular ejection fraction
RACD	= radiation-associated cardiac disease

🖰 Supplemental material is available online.

Radiation therapy is an effective treatment for many kinds of malignancies involving the mediastinum and thorax. However, over the past 30 years, the long-term deleterious effects of therapeutic radiation on the cardiovascular system have been increasingly recognized. Cardiovascular issues are now the leading causes of death in survivors of those malignancies.[1-6]

Radiation-associated cardiac disease (RACD) may present in a heterogeneous manner that can be dominated by proximal coronary artery stenoses, valvular lesions, constrictive pericarditis, myocardial disease, conduction abnormalities, or their combination.[7-11] These effects are often insidious, with symptoms occurring years after completion of the original radiation therapy. Given this long latency period before cardiac symptoms become overt, failure to recognize the impact of radiation on cardiac manifestations is common. Thus, the precise prevalence of cardiac morbidity in those who previously received therapeutic thoracic radiation is unknown, and likely depends on radiation dose, use of concomitant chemotherapy, other cardiac comorbidities, and radiation beam direction and shielding. Some studies[7,11] have suggested that the frequency of myocardial fibrosis is as high as 63%, and that the prevalence of subclinical left ventricular (LV) dysfunction ranges from 39% to 57%.

Although RACD patients often require cardiovascular surgical intervention, their postoperative morbidity and mortality is much higher than would be expected based on standard risk scores.[2,3,5,12-16] Although the cause of this discrepancy is likely multifactorial, a possible culprit is myocardial dysfunction. Radiation-associated cardiac disease may lead to myocardial dysfunction by virtue of the effects of radiation itself, which may be compounded by the use of chemotherapeutic agents with adverse cardiac effects in this population and further influenced by the ventricular dysfunction that accompanies decompensated valve disease and coronary artery disease.

Although the LV ejection fraction (EF) and volumes are valuable in estimating risk across populations when there is a wide spectrum of abnormality—from normal to severely abnormal—their prognostic value diminishes when the spectrum of abnormality is narrower. Advanced echocardiographic techniques such as speckle tracking (that enable us to measure LV strain) may be more sensitive in detecting long-axis abnormalities in myocardial mechanics, and may indicate pathology before this is evident on conventional indices of LV function.[17-19] Given the potential importance of myocardial dysfunction to surgical outcomes in patients with prior radiation exposure, we sought to: (1) determine whether LV global longitudinal strain (LV-GLS) can independently predict long-term mortality in RACD patients undergoing cardiac surgery; and (2) investigate the time-dependent changes of LV size and function after cardiac surgery in this population, by using longitudinal data analysis.

METHODS
Study Population

This was a retrospective observational study of 163 consecutive patients with RACD who underwent cardiothoracic surgery at our center between 2000 and 2003. All patients had a detailed echocardiogram performed before their surgery. From an original study population of 173 such patients, we excluded 10 patients in cases in which high-quality offline LV-GLS analysis could not be performed. All patients had a history of malignancy that required chest irradiation and who subsequently developed coronary and/or valvular disease that required cardiothoracic surgery. The diagnosis of RACD was made after a thorough clinical and echocardiographic evaluation was conducted by experienced cardiologists. In this group, type of prior malignancy and area of radiation were ascertained. When available, the year of the most recent radiation dose was recorded. In addition, the approximate radiation dosages for various malignancies were recorded, based on historic data. All patients were cleared by oncology to undergo a cardiac surgical procedure.

Clinical Data

All clinical and demographic data were assembled using electronic medical records, after appropriate approval by the institutional review board. History and type of prior cardiac surgery were recorded. A record was made of medications at the time of initial presentation, and whether these were initiated in the postoperative period. Presence of permanent atrial fibrillation, defined according to guidelines, at baseline, and at the time of discharge, was ascertained.[20] Presence of an automated implantable cardioverter defibrillator and need for a permanent pacemaker were recorded.

The details of cardiac surgery were recorded prospectively, and categorized as follows: (1) coronary artery bypass grafting (CABG); (2) CABG + 1 valve repair and/or replacement; (3) CABG + ≥2 valve repairs and/or replacements; (4) 1 valve repair and/or replacement; (5) ≥2 valve repairs and/or replacements; (6) others (including pericardiectomy, transplantation, LV assist device, aortic surgery, and myectomy). In patients that underwent CABG, the number of bypassed vessels was recorded. Based on the preoperative data, the additive EuroSCORE (European System for Cardiac Operative Risk Evaluation) was calculated to predict risk of postoperative mortality.[21]