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The risk of reoperative cardiac surgery in radiation-induced valvular disease

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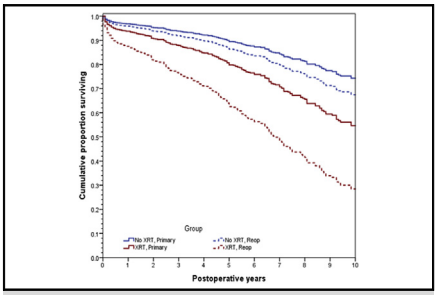
ABSTRACT

Objective: Mediastinal radiation therapy (MRT) increases the risk for adverse outcomes after cardiac surgery and is not incorporated in the Society of Thoracic Surgeons (STS) risk algorithm. We aimed to quantify the surgical risk conferred by MRT in patients undergoing primary and reoperative valvular operations.

Methods: A retrospective analysis of 261 consecutive patients with prior MRT who underwent valvular operations between January 2002 and May 2015. Short- and long-term outcomes were compared for STS predicted risk of mortality, surgery type, gender, year of surgery, and age-matched patients stratified by reoperative status.

Results: Mean age was 62.6 ± 12.1 years and 174 (67%) were women. The majority had received MRT for Hodgkin lymphoma (48.2%) and breast cancer (36%). Overall, 214 (82%) were primary and 47 (18%) were reoperative procedures. Reoperation carried a higher operative mortality than primary cases (17% vs 3.7%; $P = .003$). Compared with the 836 nonradiated matches, operative mortality and observed-to-expected STS mortality ratios were higher in primary (3.8% [1.4] vs 0.8% [0.32]; $P = .004$) and reoperative (17% [3.35] vs 2.3% [0.45]; $P = .001$) patients with prior MRT. Cox proportional hazard modeling revealed that in patients with previous MRT, primary (hazard ratio, 2.24; 95% confidence interval, 1.73-2.91) and reoperative status (hazard ratio, 3.19; 95% confidence interval, 1.95-5.21) adversely affected long-term survival compared with nonradiated matches.

Conclusions: Surgery for radiation-induced valvular heart disease has a higher operative mortality than predicted by STS predicted risk of mortality. Reoperations are associated with increased morbidity and mortality compared with primary cases. Careful patient selection is paramount and expanded indications for transcatheter therapies should be considered, especially in reoperative patients. (J Thorac Cardiovasc Surg 2017;154:1883-95)



Reoperative status was a significant predictor for long term mortality (hazard ratio, 1.92; $P = .013$).

Central Message

Surgery for radiation-induced valvular heart disease has higher mortality than predicted by Society of Thoracic Surgeons score. Reoperations are associated with increased morbidity and mortality compared with primary cases.

Perspective

This analysis of patients undergoing surgery for radiation-induced valvular heart disease shows that the Society of Thoracic Surgeons risk model does not adequately capture their operative mortality. Reoperation for radiation-induced valvular heart disease is associated with a higher operative and long-term mortality compared with primary surgery. This result should prompt careful preoperative risk evaluation and expand the indications for transcatheter valve therapies.

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Mediastinal radiation therapy (MRT) remains an effective treatment for thoracic and chest wall neoplasms, including lymphomas, breast cancer, thymomas, and lung and esophageal cancers. However, MRT carries many delayed cardiovascular adverse effects such as accelerated coronary

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Abbreviations and Acronyms

AVR = aortic valve replacement
EMR = electronic medical record
MRT = mediastinal radiation therapy
NYHA = New York Heart Association
PROM = predicted risk of mortality
STS = Society of Thoracic Surgeons
VHD = valvular heart disease

artery disease, valvular heart disease (VHD), conduction system abnormalities, pericardial constriction, and restrictive cardiomyopathy.[1-6] This risk is increased with extended radiation treatment fields and higher radiation doses, such as those used to treat Hodgkin lymphoma, testicular cancer, and thymomas.[7] VHD is estimated to develop in 6% to 15%[8] of patients who receive MRT, 11 to 16 years after its completion.[2,9] Aortic regurgitation, aortic stenosis, and tricuspid regurgitation are present in 60%, 16%, and 4% of these patients, respectively.[10,11] Aortic stenosis is the most common MRT-induced valvular abnormality requiring surgical intervention.[10]

It is known that prior MRT is associated with inferior short-term and long-term outcomes after cardiac surgery.[5,7,12,13] However, the most commonly used risk prediction algorithm in the United States, the Society of Thoracic Surgeons (STS) predicted risk of mortality (PROM), does not incorporate prior MRT into its calculations.[14,15] Although there are several reports evaluating operative outcomes for radiation-induced VHD, they are limited by their small numbers and heterogeneous cohorts.[3,5,13,16] We hypothesized that surgery for radiation-induced VHD is associated with adverse outcomes and that this risk is amplified in patients undergoing reoperative cardiac surgery. Accordingly, we compared the outcomes of patients undergoing primary and reoperative valvular operations for radiation-induced VHD to a matched cohort of primary and reoperative valvular patients without a history of MRT.

METHODS

Study Population

All adult patients aged ≥18 years who underwent valvular surgery at Brigham and Women's Hospital between January 2002 and May 2015 were identified from our electronic medical record (EMR). All patients with isolated valvular or concomitant valvular and/or coronary artery bypass graft surgery were included. Those with valvular operations for endocarditis, heart transplantation, or ventricular assist devices were excluded. A total of 261 out of 9659 (2.7%) patients underwent valvular surgery for VHD following MRT for a documented malignancy. Patients were grouped by whether it was a primary cardiac surgery (n = 214) or a redosternotomy (reoperation) (n = 47).

The indication for MRT was collected for all patients. However, the dates and doses of MRT were not reliably documented in the available EMR, predominately due to the remoteness of the MRT. The diagnosis of MRT-induced VHD was based on comprehensive clinical and imaging data as well as the expert opinion of the referring cardiologist. All patients were cleared by oncology before surgery.

Data Collection and Outcomes

Patient characteristics, perioperative data, laboratory test results, and in-hospital outcomes were recorded electronically at the time of presentation. Data were extracted from the EMR and variables were defined and coded according to the STS Adult Cardiac Surgery Database version 2.52 specifications, unless otherwise noted. The presence of meaningful coronary artery disease was defined as a ≥70% obstruction in any coronary or ≥50% in the left main coronary artery. Right ventricular dysfunction, right ventricular dilation, nonischemic cardiomyopathy, and restrictive cardiomyopathy were deemed positive if present as moderate or severe in the patients' preoperative echocardiogram. Operative mortality was defined as any death occurring in-house during the index admission, or within 30 days of surgery if discharged.

The primary outcomes of interest were operative mortality and long-term survival. Secondary outcomes included valve-related complications, perioperative morbidity, and length of stay.

Longitudinal mortality data was obtained from our internal research repository, routine patient follow-up, and our state Department of Public Health. Survival follow-up was 100% in this cohort. Follow-up time was measured in months from the date of surgery to the date of death or study end (April 30, 2016) if alive.

Partners Healthcare Institutional Review Board approved this study. Informed consent from individual patients was waived.

Statistical Analysis

Normally distributed continuous variables are expressed as mean ± standard deviation and were compared using Student t tests with Levene test for homogeneity of variance. Nonnormally distributed variables are expressed as median and interquartile range and were compared using Mann-Whitney U tests. Categorical variables are presented as number and percentage and were compared using χ^2 or Fisher exact tests. Longitudinal survival was estimated by Kaplan-Meier analyses, and groups were compared using log-rank test. A forward-stepwise Cox proportional hazard model was used to evaluate risk factors influencing survival. Continuous variables evaluated included age, creatinine (in milligrams per deciliter), and ejection fraction (as a percentage). Categorical variables included type of cancer, type of surgery, gender, vascular and cerebrovascular disease, renal insufficiency, congestive heart failure, and previous cardiac surgery. Variables selected for inclusion in the Cox model included those that were significantly associated with mortality on univariate analyses, those known to be contributors to all-cause mortality, and those with clinical importance to morbidity and mortality. All analyses were conducted using IBM SPSS Statistics version 22.0 (IBM-SPSS Inc, Armonk, NY) and $P \leq .05$ was the criterion for significance.

Matched Analysis

To better quantify the operative morbidity and mortality risks associated with MRT before reoperative valvular surgery, we sought to compare outcomes with a matched cohort. We thus first derived from our consecutive series of valve patients a pool of potential matches with the same frequency distributions for age, gender, year of surgery, and type of procedure, who had no documented history of cancer. We then selected matches on the basis of nearest STS PROM within a 0.05% caliper, followed by surgery type, gender, year of surgery, and age, stratified by reoperative status. The intended goal was 3 to 4 matches per MRT patient; however, all matches with exact STS PROM (to 4 decimal places), procedure, and gender were retained. A total of 1049 matched patients were identified; 836 primary patients without MRT (3.2 matches per MRT patient) and 213 reoperative patients (5.7 matches per reoperative