Percutaneous revascularization in patients treated with thoracic radiation for cancer

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Objectives To assess coronary revascularization outcomes in patients with previous thoracic radiation therapy (XRT).

Background Previous chest radiation has been reported to adversely affect long term survival in patients with coronary disease treated with percutaneous coronary interventions (PCI).

Methods Retrospective, single center cohort study of patients previously treated with thoracic radiation and PCI. Patients were propensity matched against control patients without radiation undergoing revascularization during the same time period.

Results We identified 116 patients with radiation followed by PCI (XRT-PCI group) and 408 controls. Acute procedural complications were similar between groups. There were no differences in all-cause and cardiac mortality between groups (all-cause mortality HR 1.31, $P = .078$; cardiac mortality 0.78, $P = .49$).

Conclusion Patients with prior thoracic radiation and coronary disease treated with PCI have similar procedural complications and long term mortality when compared to control subjects. (Am Heart J 2017;187:98-103.)

Cancer survival has substantially improved with advances in modern therapies. As the population of long term cancer survivors has increased, there has been a growing recognition of the delayed deleterious effects of cancer therapies. Thoracic external beam radiation therapy (XRT) is associated with later development of cardiovascular disease including coronary artery disease.[1,2] Historically, 50% of Hodgkin lymphoma survivors treated with mediastinal XRT developed cardiac disease, with cardiac disease accounting for 25% of the total mortality observed in this cohort.[2] In breast cancer survivors thoracic radiation has been associated with a 1.76-fold (95% CI: 1.34 to 2.31) higher risk of dying from cardiac disease as compared to controls.[1]

The role of percutaneous coronary intervention (PCI) has been well established in the general population. However, outcomes in cancer survivors with previous thoracic radiation exposure remain unknown. We have previously shown that thoracic radiation prior to or following PCI does not increase the risk of late stent failure.[5] Given the durability of PCI in this cohort and the risk for subsequent progressive valve and pericardial disease which may necessitate a second sternotomy, catheter-based therapies may be the preferred method of revascularization, particularly when an acceptable internal mammary artery (IMA) conduit is not available. However, important questions remain including how radiation impacts procedural complications and long term survival following PCI. The aim of our study was to assess short term complications and long term survival following PCI in radiation treated patients.

Methods

Study population

This was a single center, retrospective cohort study of patients who received thoracic radiation and percutaneous coronary revascularization for CAD at the Mayo Clinic (Rochester, MN). 30,900 patients received thoracic radiation between 1971 and 2013. 16,578 patients underwent PCI from 1994 to 2013. After cross referencing the two patient lists, 155 patients were identified who underwent radiation prior to PCI. Next, patients

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Table I. Location and type of cancer in the study cohorts

Cancer type, N (%)	N = 116
Breast	59 (51)
Esophageal	13 (11)
Hodgkin lymphoma	11 (9)
Non-Hodgkin's lymphoma	3 (3)
Lung	19 (16)
Mediastinum	3 (3)
Thoracic spinal cord	1 (1)
Stomach	3 (3)
Thyroid	4 (3)
> 1 type of cancer	1 (1)

were excluded if the radiation field did not involve the heart or if they were treated with palliative intent radiation. Propensity matched controls were selected from patients treated with PCI over the same time period but without previous thoracic radiation exposure. Propensity score matching was performed on multiple clinical and procedural factors which are available in Supplemental Table I.

Radiation therapy

All patients had a diagnosis of cancer (biopsy proven or radiographically early stage non-small cell lung cancer), and were treated with curative intent radiation including standard or intensity-modulated radiotherapy (Table I). Over 90% of patients received radiation for lymphoma, breast, lung, or esophageal cancer. A radiation oncologist reviewed all computed tomography radiation simulation plans and confirmed cardiac involvement for each patient.

PCI database

The Mayo Clinic PCI registry includes demographic, angiographic, and procedural data for patients treated with PCI at our institution. In-hospital events are recorded, and follow up data including all-cause and cardiac mortality is obtained via telephone contact by a research coordinator using a questionnaire at 6 months, 1 year, and then annually. Patients with angioplasty and/or stenting from 1994–2013 (including bare metal and drug eluting stents) were included. All patients were prescribed dual antiplatelet therapy (1 month for bare metal stents, 12 months for drug eluting stents), and lifelong aspirin therapy was recommended.

Outcomes

The primary outcome was all-cause mortality. Secondary outcomes included cardiac and non-cardiac mortality and procedural characteristics including complications, the number and location of diseased vessels, number of vessels intervened on, number and type of stents deployed, and angiographic characteristics.

Statistical methods

Continuous variables are summarized as mean ± SD. Discrete variables are summarized as a frequency (percentage). A propensity score was created using logistic regression (Supplemental Table I). Optimal variable matching was used with up to 4 reference subjects matched to each radiation patient.[6] Reference subjects were chosen according to age (within 5 years), gender, date of revascularization (within 2 years), and propensity score (within 1/4 the SD of the propensity score distribution). When calculating descriptive statistics, weighting was used to account for the different number of referent subjects matched to each radiation case. Conditional logistic regression was used to test the difference between radiation subjects and their matched controls. Kaplan–Meier methods were used to estimate all-cause mortality. Competing-risks methods were used to estimate the incidence of cause-specific mortality. To test differences in survival, Cox proportional hazards models were applied with a frailty term for each set of matched subjects. Follow-up time was measured starting from the date of revascularization to date of death or censor. All analyses were performed using SAS version 9.3 or higher (SAS Inc, Cary, NC). All hypotheses tests were 2-sided with a 0.05 significance level.

This study was conducted with institutional review board approval. No extramural funding was used to support this work. The authors are solely responsible for the design and conduct of this study, the study analysis, and drafting and editing of the paper.

Results

Percutaneous coronary intervention

A total of 116 cancer survivors previously treated with thoracic radiation underwent PCI (XRT-PCI patients). The median radiation to PCI interval was 5.6 years (interquartile range [IQR] 1.1, 12.3 years). We identified 408 propensity matched control patients. Baseline and demographic characteristics for can be found in Table II, while angiographic and procedural characteristics are outlined in Table III. Patients were well matched on both clinical and angiographic variables. Compared with controls, XRT-PCI patients had less hypertension (73% vs 83%, $P = .025$) and more often had an ejection fraction ≤40% (18% vs 13%, $P = .043$). Previous radiation did not result in a higher rate of PCI complications (Table III).

After a median follow-up of 6.3 years after PCI (IQR 4.0, 9.8 years), there was no difference in all-cause, cardiac, or non-cardiac mortality between XRT-PCI patients and controls (Figure A-B). Fifty-six deaths occurred in the XRT-PCI group (including 12 due to cardiac causes), and 159 deaths occurred in the controls (including 44 cardiac deaths).