Lung

Association of Left Anterior Descending Coronary Artery Radiation Dose With Major Adverse Cardiac Events and Mortality in Patients With Non-Small Cell Lung Cancer

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IMPORTANCE

Radiotherapy accelerates coronary heart disease (CHD), but the dose to critical cardiac substructures has not been systematically studied in lung cancer.

OBJECTIVE

To examine independent cardiac substructure radiotherapy factors for major adverse cardiac events (MACE) and all-cause mortality in patients with locally advanced non-small cell lung cancer (NSCLC).

DESIGN, SETTING, AND PARTICIPANTS

A retrospective cohort analysis of 701 patients with locally advanced NSCLC treated with thoracic radiotherapy at Harvard University-affiliated hospitals between 1 December 2003, and 27 January 2014, was performed. Data analysis was conducted between 12 January 2019, and 22 July 2020. Cardiac substructures were manually delineated. Radiotherapy dose parameters (mean, maximum, and the volume [V, percentage] receiving a specific Gray [Gy] dose in 5.0-Gy increments) were calculated. Receiver operating curve and cut-point analyses estimating MACE (unstable angina, heart failure hospitalisation or urgent visit, myocardial infarction, coronary revascularisation, and cardiac death) were performed. Fine and Gray and Cox regressions were adjusted for pre-existing CHD and other prognostic factors.

MAIN OUTCOMES AND MEASURES

MACE and all-cause mortality.

RESULTS

Of the 701 patients included in the analysis, 356 were men (50.8%). The median age was 65 years (interquartile range, 57-73 years). The optimal cut points for substructure and radiotherapy doses (highest C-index value) were left anterior descending (LAD) coronary artery V15 Gy greater than or equal to 10% (0.64), left circumflex coronary artery V15 Gy greater than or equal to 14% (0.64), left ventricle V15 Gy greater than or equal to 1.0% (0.64), and mean total coronary artery dose greater than or equal to 7 Gy (0.62). Adjusting for baseline CHD status and other prognostic factors, an LAD coronary artery V15 Gy greater than or equal to 10% was associated with increased risk of MACE (adjusted hazard ratio, 13.90; 95% CI, 1.23-157.21; P = .03) and all-cause mortality (adjusted hazard ratio, 1.58; 95% CI, 1.09-2.29; P = .02). Among patients without CHD, associations with increased one-year MACE were noted for LAD coronary artery V15 Gy greater than or equal to 10% (4.9% vs 0%), left circumflex coronary artery V15 Gy greater than or equal to 14% (5.2% vs 0.7%), left ventricle V15 Gy greater than or equal to 1.0% (5.0% vs 0.4%), and mean total coronary artery dose greater than or equal to 7.0 Gy (4.8% vs 0%) (all P ≤ .001), but only a left ventricle V15 Gy greater than or equal to 1.0% increased the risk among patients with CHD (8.4% vs 4.1%; P = .046). Among patients without CHD, two-year all-cause mortality

was increased with an LAD coronary artery V15 Gy greater than or equal to 10% (51.2% vs 42.2%; P = .009) and mean total coronary artery dose greater than or equal to 7.0 Gy (53.2% vs 40.0%; P = .01).

CONCLUSIONS AND RELEVANCE

The findings of this cohort study suggest that optimal cardiac dose constraints may differ based on preexisting CHD. Although the LAD coronary artery V15 Gy greater than or equal to 10% appeared to be an independent estimator of the probability of MACE and all-cause mortality, particularly in patients without CHD, left ventricle V15 Gy greater than or equal to 1.0% appeared to confer an increased risk of MACE among patients with CHD. These constraints are worthy of further study because there is a need for improved cardiac risk stratification and aggressive risk mitigation strategies.