Effect of radiotherapy for breast cancer on the prognosis of a subsequent myocardial infarction

Naomi B. Boekel¹, Lynly Y. Boekel¹, Judy N. Jacobse¹, Michael Schaapveld¹, Maartje J. Hooning², Caroline M. Seynaeve², Margreet H.A. Baaijens³, Gabe S. Sonke⁴, Emiel J.T. Rutgers⁵, Nicola S. Russell⁶, Berthe M.P. Aleman⁶,*, Flora E. van Leeuwen¹,*

*Authors contributed equally to this work.

¹Netherlands Cancer Institute, Epidemiology, Amsterdam, The Netherlands
²Erasmus MC- Cancer Institute, Medical Oncology, Rotterdam, The Netherlands
³Erasmus MC- Cancer Institute, Radiation Oncology, Rotterdam, The Netherlands
⁴Netherlands Cancer Institute, Medical Oncology, Amsterdam, The Netherlands
⁵Netherlands Cancer Institute, Surgery, Amsterdam, The Netherlands
⁶Netherlands Cancer Institute, Radiation Oncology, Amsterdam, The Netherlands

Email: n.boekel@nki.nl

Background

Breast cancer patients treated with radiotherapy (RT) appear to have more vulnerable plaques and an increased risk of a subsequent myocardial infarction (MI). It is, however, unclear whether RT also influences the prognosis of these MIs.

Methods

We selected patients diagnosed with MI following RT from our hospital-based cohort of early breast cancer patients aged <71 years, treated 1970-2009, and extracted detailed oncologic information. Cardiovascular disease (CVD) incidence and cause of death were acquired through questionnaires to general practitioners and cardiologists.

Highest whole heart doses in breast cancer RT are mostly caused by internal mammary chain (IMC) irradiation. Hence, patients were compared based on receipt of IMC RT (IMC yes/no). Cumulative incidences were estimated for cardiac death, death due to MI and CVD incidence following MI. Death due to other causes was used as competing risk. Outcomes were also evaluated using Cox proportional hazard models adjusted for possible confounders (incl. chemotherapy, CVD risk factors, CVD history, and year of MI).

Results

A total of 398 patients were included (62% IMC, 38% no IMC) with a median age of 67 years at MI diagnosis. Median time between breast cancer and MI was 15 years.

Compared to patients with no IMC RT, IMC RT patients more often died on the day of MI (20% vs. 11%,
Ten-year cumulative incidence of cardiac death was 35% for IMC patients (95% confidence interval [CI] 29-41) compared to 24% (95%CI 17-31) for patients with no IMC RT (p=0.04).

After correction for confounders, IMC RT remained associated with a higher cardiac death rate compared to no IMC irradiation (hazard ratio [HR]=1.7, 95%CI 1.1-2.5). Rates of death due to MI (HR=1.3, 95%CI 0.8-2.0) and of valvular heart disease after MI (HR=1.7, 95%CI 0.9-3.2) were nonsignificantly increased after IMC RT. At the GCOS2017 comparisons with general population rates will also be presented.

**Conclusion**

IMC RT appears to increase the cardiac death rate following MI. Although further studies are needed, our results suggest that RT may not only increase the risk of MI, but may also worsen MI prognosis. These results stress the importance of cardiac surveillance in patients with high heart doses.

Wordcount: 1,994 out of 2,000 characters (including title, excluding spaces)