Cardiotoxicity of radiotherapy in breast cancer patients

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Many randomised trials over the past half century studied the effects of breast cancer radiotherapy. They show that radiotherapy after breast-conserving surgery and after mastectomy in node-positive women reduces the risk of breast cancer recurrence and death and improves overall survival [1, 2]. However, breast cancer radiotherapy inevitably involves some radiation exposure of the normal tissues which can result in adverse effects such as heart disease.

Oncologists need information on the absolute risk of radiotherapy-related heart disease for women irradiated today. This requires studies which include large numbers of women, with data on non-fatal as well as fatal cases, cardiac risk factors at the time of cancer treatment and information on radiation dose to the heart. Women with left-sided breast cancer typically receive higher cardiac radiation doses than women with right-sided breast cancer, so observational studies comparing heart disease rates in women with left- and right-sided primary tumours may provide an unbiased assessment of the difference in cardiac risk.

Using information on hospital discharge diagnoses for a cohort of 35,000 women who received radiotherapy for breast cancer in Denmark and Sweden we showed that the incidence ratio, left-sided versus right-sided, was raised for all heart diseases combined (1.08; 95% CI: 1.02–1.15; $p = 0.01$). It was also raised for the individual diagnoses of ischaemic heart disease, pericarditis and valvular heart disease [3].

This cohort was used as a basis of a population-based case-control study of major coronary events (MCEs, i.e., diagnosis of myocardial infarction, treatment with coronary revascularization or death from ischaemic heart disease) after radiotherapy. Mean radiation dose to each woman's heart was estimated and we found that the MCE [4] rate increases approximately linearly with mean heart dose by 7.4% per Gy (95% CI: 2.9–14.5; $p < 0.001$) with no apparent threshold. The increase started within 5 years of radiotherapy and continued into the third decade. The percentage increase in MCE rate per Gy was similar in women with and without cardiac risk factors at the time of radiotherapy. It did not differ significantly according to any other patient or tumour characteristics for which information was available or according to other cancer treatments that the women received.

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Although radiotherapy practice has changed over the past few decades and heart doses have reduced substantially, there is still need for further research on the cardiac effects of radiotherapy. In particular, more information on the risks of cardiac conditions such as valvular disease after radiotherapy and also on the risks of radiotherapy in women who also receive chemotherapy are necessary. Full assessment of the absolute risks and benefits will mean that treatments with the greatest net benefits can be chosen for individual patients in the clinic.

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All authors equally contributed to idea & design of the article, clinical data collection, analysis of the data and writing the manuscript.