

Risk of Radiation-related Heart Disease in 1 Million Irradiated Breast Cancer Patients

Katherine Henson, Sarah C. Darby and Paul McGale, Clinical Trial Service Unit (CTSU), University of Oxford on behalf of the Collaborative Group on Observational Studies of Breast Cancer

BACKGROUND

Radiotherapy can reduce the risk of breast cancer recurrence and of death from breast cancer, but it often involves some incidental irradiation of the heart and so can increase the risk of heart disease.

Many factors influence a woman's risk of heart disease and so comparisons of heart disease rates in irradiated and unirradiated women cannot be used to study the risk of radiation-related heart disease. However, the positioning of the heart means that it usually receives a higher radiation dose from treatment for left-sided breast cancer than for right-sided breast cancer. Thus, a comparison of mortality from heart disease in irradiated women with left and right-sided breast cancer is an effective way of investigating the risk of fatal heart disease attributable to radiotherapy.

MATERIALS & METHODS

- 87 registries in 40 countries have contributed information on cause-specific mortality for women diagnosed with breast cancer to the Collaborative Group on Observational Studies of Breast Cancer Survivors
 - Aged between 20 and 79 years at breast cancer diagnosis
 - Diagnosed in the period 1935-2008
 - Of known breast cancer laterality and radiotherapy status
- Each woman's contribution to the person-years at risk ran from the date of breast cancer diagnosis to the earliest occurring event of death, loss to

- follow-up, 95th birthday, or end of follow-up period for the registry
- The deaths and person-years were stratified by:
 - Years since radiotherapy (5-year groups)
 - Calendar year of radiotherapy (5-year groups)
 - Age at radiotherapy (5-year groups)
 - Country of treatment
- Mortality ratios, left-sided versus right-sided, were estimated using grouped logistic regression

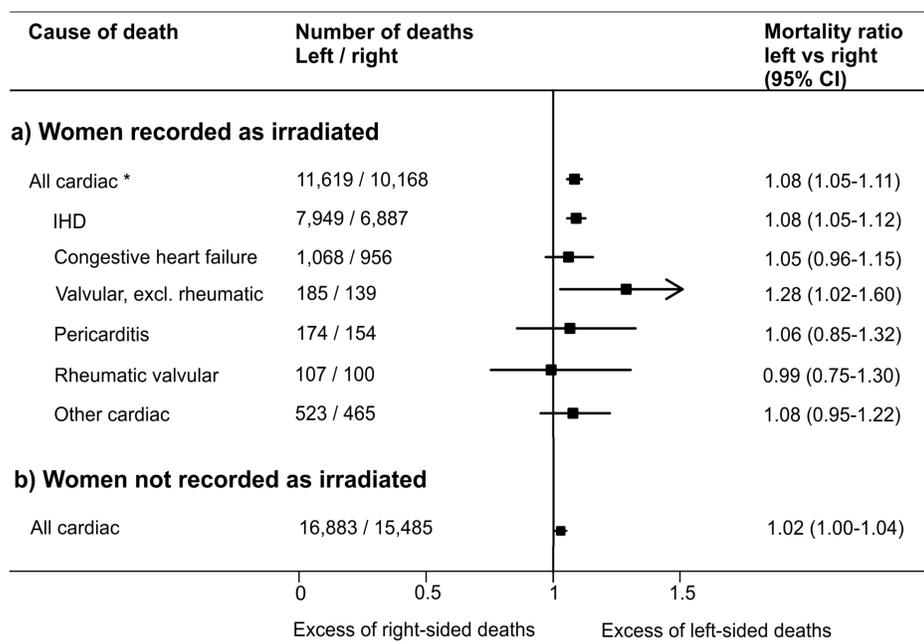
RESULTS

- There were a total of 1,923,362 women
- 1,000,148 women (53%) were recorded as receiving radiotherapy
- 53,555 women had died of heart disease
- The mortality ratio, left-sided versus right-sided, for women recorded as irradiated was 1.08 (95%CI: 1.05 - 1.11) for all types of heart disease combined
- Among irradiated women there were significant left-sided excesses for valvular disease and IHD when considered separately
- Among women not recorded as irradiated, there was no comparable left-sided excess for all types of heart disease combined

Among women recorded as irradiated, the increased mortality after left-sided compared with right-sided breast cancer, for all types of heart disease combined:

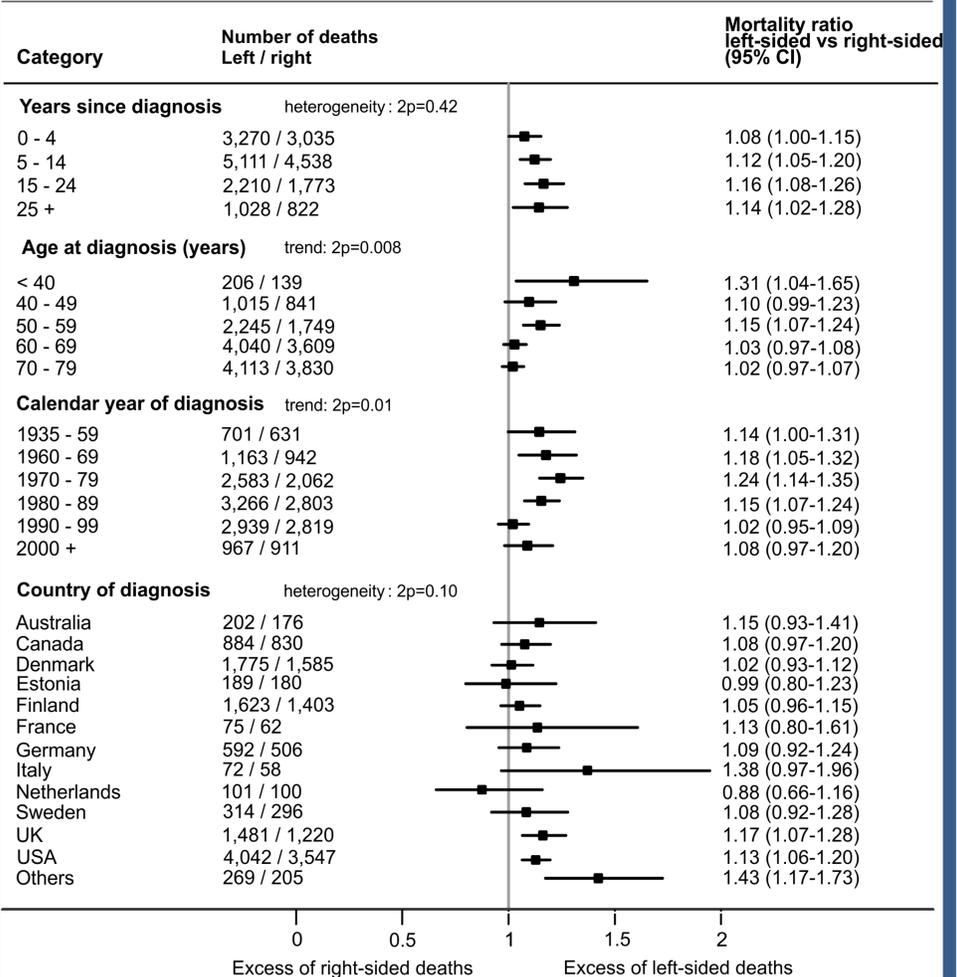
- started during years 0-4 and was still present at years 25+
- was proportionately larger for younger women
- is lower for women treated more recently
- appears to have affected many countries

Mortality ratios, left-sided versus right-sided breast cancer, for women recorded as irradiated and other women by cause of death



* Numbers of deaths for specific cardiac diseases do not add up to total number of cardiac deaths as not all specific registries provided information on specific causes

Mortality ratios, left-sided versus right-sided breast cancer, for women recorded as irradiated for different categories for all heart disease combined



CONCLUSIONS

The study shows that:

- the excess cardiac mortality in women irradiated for left-sided breast cancer is mainly due to IHD and valvular heart disease
- the proportional increase is highest for younger women
- the risks from modern radiotherapy are lower than in earlier years
- the increased risk begins within the first five years following radiation and continues into the third decade since treatment

