

History of myocardial infarction (MI) increases the risk of radiation-induced MI in women with breast cancer

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Background

In early breast cancer, radiotherapy has been shown to reduce tumor-related mortality but, for some past regimens, this reduction has been offset by increased mortality from radiation-induced MI¹. For most regimens, the dose of radiation received by the heart is larger for left-sided than for right-sided tumors. Therefore, the effect of radiotherapy on subsequent MI can be studied in observational data by comparing the subsequent health of irradiated women with left-sided breast tumors to those with right-sided tumors.^{2,3}

Objective

At present, little is known about the factors that influence the risk of radiation-induced MI. In the general population, people with a history of MI are known to be at increased risk of another MI in the future. We have therefore investigated whether the risk of radiation-induced MI is increased for women with a history of MI before their breast cancer.

Material and methods

Tumor laterality, whether or not radiotherapy was given, and other basic information was collated for women diagnosed with breast cancer in Denmark during 1977-2000 and in the Stockholm and Umeå regions of Sweden during 1976-2001, see Table 1.

Table 1. Characteristics of study population

	Breast cancer laterality			
	Right		Left	
	Number of women	% with radiotherapy	Number of women	% with radiotherapy
Denmark	21,797	42 %	23,283	42 %
Sweden	8,671	63 %	9,202	63 %
Total	30,468	48 %	32,485	48 %

History of MI before breast cancer

The women were cross-matched with hospital disease registers, which have been nationwide in Denmark and Sweden since the mid-1970s, to ascertain which women had a history of MI before their breast cancer. 1.1% of women had, and this did not vary with the laterality of the breast cancer, see Table 2.

Table 2. Numbers of women with a history of MI before their breast cancer

History of MI before breast cancer	Breast cancer laterality	
	Right	Left
No	30,136 (98.9 %)	32,119 (98.9 %)
Yes	332 (1.1 %)	336 (1.1 %)
Total number of women	30,468 (100 %)	32,485 (100 %)

MI after breast cancer

Further cross-matches with the hospital disease registers ascertained which women had MI after their breast cancer, and cross-matches with nationwide-death registers established which women had died and their cause of death, see Table 3.

Table 3. Numbers of women with MI after breast cancer, or who had died

	Number of women	% with radiotherapy
a. Fatal or non-fatal MI after breast cancer	2,244	41 %
b. Not in a. and died from a cause other than breast cancer	10,379	39 %
c. Not in a. and died from breast cancer	16,570	51 %
Total number of women with MI after breast cancer, or who had died	29,193	46 %

Mortality without MI after breast cancer

Among women with no MI after their breast cancer, the mortality ratios, left-sided versus right-sided, were close to one, regardless of whether or not the woman had a history of MI before her breast cancer and regardless of whether or not she had radiotherapy, see Table 4.

Table 4. Mortality ratios, left-sided vs right-sided breast cancer, for all causes of death in women with no MI after their breast cancer

History of MI before breast cancer	Radiotherapy for breast cancer	
	No	Yes
No	0.99 (0.96, 1.02)	1.03 (0.99, 1.06)
Yes	1.05 (0.80, 1.38)	1.15 (0.79, 1.68)
p for difference	0.6	0.5

MI after breast cancer

For unirradiated women, the rate ratio, left-sided versus right-sided, for MI after breast cancer was non-significantly less than one, whether or not the woman had a history of MI before her breast cancer, see Table 5.

For irradiated women with no history of MI before their breast cancer, the rate ratio left-sided versus right-sided, for MI after breast cancer was 1.12 (95% CI 0.98, 1.28, p=0.1). Although not significantly raised, this increase is similar to that reported in studies with larger numbers.^{2,3}

For irradiated women with a history of MI before their breast cancer, the rate ratio, left-sided versus right-sided for MI after breast cancer was 2.11 (95% CI 1.26, 3.52, p=0.005). This was significantly higher (p=0.02) than the ratio for irradiated women with no history of MI before their breast cancer.

Table 5. Rate ratios, left-sided vs right-sided breast cancer, for fatal or non-fatal MI after breast cancer, and 95% CIs

History of MI before breast cancer	Radiotherapy for breast cancer	
	No	Yes
No	0.98 (0.88, 1.10)	1.12 (0.98, 1.28)
Yes	0.74 (0.50, 1.12)	2.11 (1.26, 3.52)
p-for difference	0.20	0.02

Conclusion

The risk of radiation-induced MI may be particularly increased for women with a history of MI at the time of their breast cancer.

References

1. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. *Lancet* 2005; 366: 2087-2106.
2. Darby SC, McGale P, Peto R, Granath F, Hall P, Ekbom A. Mortality from cardiovascular disease more than 10 years after radiotherapy for breast cancer: nationwide cohort study of 90 000 Swedish women. *British Medical Journal* 2003; 326: 256-257.
3. Darby SC, McGale P, Taylor CW, Peto R. Long-term mortality from heart disease and lung cancer after radiotherapy for early breast cancer: prospective study of about 300 000 women in US SEER cancer registries. *Lancet Oncol* 2005; 6: 557-565.