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HRT and the efficacy of mammographic screening for breast cancer

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Hormone replacement therapy, interval cancer, mammography, sensitivity, specificity

Introduction

Existing evidence suggests that use of HRT detrimentally affects the accuracy of mammographic screening for breast cancer. Use of HRT is common in the age group invited to routine mammographic screening.

Aims

To examine the sensitivity, specificity and small invasive breast cancer detection rate according to HRT use in a population-based study of women aged 40 and over.

Comments

This study adds to the increasing body of evidence demonstrating a decrease in the sensitivity and specificity of mammographic breast cancer screening in current hormone replacement therapy (HRT) users, compared to non-users. Since HRT use is common in women attending breast cancer screening and has also been shown to increase the risk of breast cancer itself, this has important implications for screening programmes and for women attending them. In common with all but one of the studies investigating the relationship between HRT use and the accuracy of mammographic screening, this study was not able to control for important potential confounding factors, including menopausal status. Nevertheless, the broad finding of an increased risk of interval cancer and 'false positive' screens in women currently using HRT is likely to be real.

Methods

BreastScreen Victoria (Australia) offers free mammographic screening to women aged 40 and over and specifically invites women aged 50 to 69 for screening approximately once every two years.

Screening consists of two-view mammography. A total of 103,770 women attending their first mammographic screen in 1994 were followed for their screening outcome and for the development of invasive breast cancer in the two years following this screen (i.e. interval cancer or false negative), using the regional cancer registry and screening records. HRT use (use versus non-use), family history of breast cancer and symptom status were ascertained using a self-administered questionnaire at the time of screening. Women with a past history of breast cancer and those with a breast lump or bloodstained or watery nipple discharge at the time of screening were excluded. The relationship between current HRT use versus non-use and screening accuracy was then assessed according to the risk of interval versus screen-detected cancer (related to sensitivity), the risk of being referred for assessment following screening with no subsequent diagnosis of breast cancer (related to specificity) and the proportion of women diagnosed with screen-detected cancers measuring 10 mm or less. Unconditional logistic regression modelling was used to adjust for age, family history of breast cancer and symptom status.

Results

In the entire study group, 27% of women were currently using HRT. Based on a two year screening interval, the crude sensitivity of mammographic screening was 64.8% (95% CI = 58-72) in current HRT users and 77.3% (95% CI = 74-81) in non-users.

HRT users were significantly more likely to have an interval cancer (false negative) than non-users (odds ratio 1.60 [1.04-2.21]), adjusting for age, family history of breast cancer and symptom status. The crude specificity of screening was 94.5% (95% CI = 94.2-94.8) in HRT users and 95.1% (95% CI = 94.9-95.1) in non-users. Amongst women without breast cancer, the adjusted odds ratio for a false positive screen (current HRT users versus non-users) was 1.12 (95% CI = 1.05-1.19). When restricted to the agegroup invited for screening (50-69 years), the sensitivity of mammography was 64.3% (95% CI = 57-72) in HRT users and 79.8% (95% CI = 76-84) in non-users. There was no significant difference between current HRT users and non-users with respect to small cancer detection rates.

Discussion

Compared to non-use, current HRT use was associated with reduced sensitivity and specificity of screening mammography. Twenty percent more cancers would have been detected in current HRT users if the sensitivity was the same as that for non-users. The decrease in the accuracy of screening is in keeping with other studies on the subject and the most likely explanation for this finding is that HRT use increases mammographic density.

However, the study did not collect information on many reproductive, demographic and menopause related factors, and the possibility of residual confounding cannot be excluded. The effect of HRT may

be rapidly reversible and in future women could be advised to cease use prior to screening. The widespread use of HRT may undermine the ability of breast screening programmes to reduce breast cancer mortality in the long term. Women should be given information on the detrimental effect of HRT on the accuracy of mammographic screening when they are deciding whether or not to use it.

References

1. Kavenagh AM, Mitchell H, Giles GG: Hormone replacement therapy and accuracy of mammographic screening. *Lancet*. 2000, 355: 270-274.