EFFECTS OF MENOPAUSAL HORMONE THERAPY AND THE RISKS OF SCREEN DETECTED AND INTERVAL BREAST CANCERS IN A LARGE UK PROSPECTIVE STUDY

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Background The use of hormone therapy for the menopause (HT) has been shown to affect the sensitivity and specificity of mammographic screening. However there is little evidence on how the association between HT use and risk of screen detected breast cancer compares with that of interval breast cancer. We examined these associations in a large UK prospective study.

Methods We used Cox proportional hazard models to estimate the relative risk (RR) of screen detected and of interval cancer in relation to HT use among post-menopausal women who attended for routine mammographic screening. Analyses were stratified by year of birth and year of recruitment and adjusted for relevant confounders including socio-economic status, reproductive history, anthropometric and other lifestyle factors.

Results Of the 1,076,203 eligible women in the cohort, 14,730 were diagnosed with a screen-detected cancer and 8,659 with an interval breast cancer. When compared to non-users of HT, current-or-recent users were at a much higher risk of an interval cancer (RR=2.18, 95%CI 2.07–2.30) than of a screen detected cancer (RR=1.44, 95%CI 1.38–1.51). For oestrogen only HT, the corresponding RRs and 95% CI for interval and screen-detected cancers were 1.60(1.48–1.73) and 1.11(1.05–1.19); and for oestrogen and progesterone HT, the corresponding values were 2.75(2.58–2.92) and 1.79(1.70–1.88).

Conclusion In this large cohort of UK women, current-or-recent users of HT were at a substantially higher risk of being diagnosed with an interval cancer than with a screen detected cancer. The difference in risk between screen-detected and interval cancer was apparent for HT preparations containing oestrogen only and combinations of oestrogen and progesterone.

INCREASED INCIDENCE OF HYPOTHYROIDISM IN BREAST CANCER SURVIVORS – A DANISH POPULATION-BASED MATCHED COHORT STUDY

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Background Research suggests increased risk of hypothyroidism among breast cancer survivors, but whether this risk is modified by treatment modalities is unclear. We estimated the incidence of hypothyroidism in breast cancer survivors, and in strata of treatment modalities.

Methods Using nationwide registries, we identified all Danish women aged ≥35 years with non-metastatic breast cancer diagnosed from 1996 through 2009. Each breast cancer survivor was matched with up to five cancer-free women (hereafter ‘controls’) on birth year and area of residence. We excluded all women with prevalent hypothyroidism or hyperthyroidism. We considered cancer-directed treatment as the receipt of chemotherapy (yes/no), with or without radiotherapy—either to the chest wall only or with addition of the lymph nodes. Hypothyroidism was defined using diagnostic codes, and/or levothyroxine prescriptions. We calculated incidence rates (IR) of hypothyroidism per 1000 person-years and associated 95% confidence intervals (CI), and estimated hazard ratios (HR) and 95%CI of hypothyroidism using Cox regression, adjusting for comorbidities.

Results We included 45,514 breast cancer survivors and 209,195 matched controls with 2,631,488 person-years of follow-up. Median follow-up was 8.4 years in the breast cancer cohort, and 10.6 years in the control cohort. Median age in both cohorts was 61 years. Breast cancer survivors had more comorbidities than the matched controls. Breast cancer survivors had higher incidence of hypothyroidism than matched controls [IR=4.3 (95%CI=4.2, 4.5), and 3.8 (95%CI=3.7, 3.9), respectively], corresponding to an adjusted HR of 1.15 (95% CI=1.09, 1.21). Breast cancer survivors who received radiotherapy to the lymph nodes with or without chemotherapy had highest risk of hypothyroidism when compared with matched controls [HR=1.66 (95%CI=1.43, 1.93) and HR=1.27 (95% CI=1.10, 1.46), respectively]. This pattern was also evident when comparing breast cancer survivors who received radiotherapy to the lymph nodes with or without chemotherapy with breast cancer survivors who did not undergo radiotherapy or chemotherapy (HR=1.65 (95%CI=1.41, 1.94) and HR=1.37, 95%CI=1.18, 1.58), respectively.

Conclusion Breast cancer survivors treated with radiotherapy to the lymph nodes had excess risk of hypothyroidism compared with age-matched women from the general population, and when compared with breast cancer survivors who do not undergo nodal radiotherapy. The risk of hypothyroidism was particularly high among patients treated with both nodal radiotherapy and chemotherapy. Our findings support systematic screening for hypothyroidism during follow-up among breast cancer survivors who receive nodal radiotherapy, and especially those who receive nodal radiotherapy and chemotherapy.