S12. BOTH MODE OF DETECTION AND HORMONE REPLACEMENT THERAPY AFFECT BREAST CANCER CHARACTERISTICS IN POSTMENOPAUSAL WOMEN

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Introduction: Observational studies, linking characteristics of breast cancer with hormone replacement therapy (HRT), have given mixed results. Overall, most report favourable stage and prognostic characteristics, with a predominance of receptor-positive breast cancers. In the "World Health Initiative" randomised trial, breast cancers that occurred among women using combined HRT, did not have such favourable characteristics [2]. The "Million Women Study" confirmed that current use of HRT is associated with an increased risk of invasive breast cancer. This effect is substantially greater for combined HRT [1]. Kerlikowske and colleagues [3] specifically looked at prognostic characteristics of breast cancer among HRT-users in a screened population. This study also demonstrates an increased risk for women using combined HRT for a long duration. The risk was increased both for tumours with favourable and unfavourable prognostic characteristics.

We looked at the effect of HRT on tumour characteristics, and examined whether mode of detection affected this, by comparing tumour characteristics of screen-detected and palpable tumours, both in HRT-users and non-users.

Patients and methods: During one year, from September 2002 onwards, we prospectively collected demographic data in all postmenopausal women who underwent primary surgery for invasive breast cancer (N=362). Exclusion criteria were "ever-use" of HRT (>1 year before diagnosis, N=31) and bilateral breast cancer (N=4). For this analysis, 327 women were eligible, of whom 42.8% were using HRT. We looked at the effect of HRT and compared mean values for age, mode of detection, histological type, size, grade, Nottingham Prognostic Index (NPI), nodal and receptor status.

Results: We looked at the two subgroups: HRT-users (N=144) versus non-users (N=183), to evaluate the effect of HRT use on tumour characteristics.

HRT-users were significantly younger when diagnosed with breast cancer (58.8 versus 67.3 years, P<0.001), had more screen-detected cancers (56.3% versus 38.8%, P=0.002) and a lower NPI (3.86 versus 4.33, P=0.001). HRT-users had significantly more grade I tumours (23.8% versus 11.5%), and less grade II tumours (28.7% versus 45.6%, P=0.001).

There was no significant difference in the percentage of invasive lobular carcinoma ($\pm 14\%$, P=0.923), size of the lesions (25.28 *versus* 27.36 mm, P=0.382), nodal status (25% *versus* 32.2%, P=0.177) or receptor status.

To evaluate the effect of HRT, we looked at the two subgroups, palpable versus screen-detected tumours, and stratified for HRT use.

In the subgroup of palpable tumours (N=175; HRT-users, N=63), we found that HRT-users were younger (59.3 versus 69.8 versus 69.0.001), had a lower NPI 4.23 versus 4.76, P=0.006) and more grade I (22.2% versus 5.4%) and less grade III lesions (38.1% versus 56.3%, P=0.002), but had tumours with the same size (28.98 versus 33.01 mm, P=0.474) and had the same nodal status (36.5% N positive versus 43.8%, P=0.424).

In the subgroup of screen-detected tumours (N=152; HRT-users, N=81), we found that HRT-users were younger (58.1 versus 62.9 years, P<0.001), but the tumours had the same size (22.45 versus 18.46 mm, P=0.261), NPI (3.58 versus 3.63, P=0.775), grade (25.0% versus 21.4% yearsus 9.8% yearsus 50.0% yearsus 11.3% yearsus 28.6% yearsus 29.6% yearsus 29.8%

To evaluate the effect of screening, we looked at the two subgroups, HRT-users versus never-users of HRT, and stratified for mode of detection. In the subgroup of HRT users (*N*=144), we found that screen-detected breast cancers (*N*=81) had a lower NPI (3.58 versus 4.23, *P*=0.004) and less positive lymph nodes (16% versus 36.5%, *P*=0.006), but the tumours had the same size (22.45 versus 28.98 mm, *P*=0.104), grade (25.0% versus 22.2% grade I, 53.8% versus 39.7% grade II, 21.3% versus 38.1% grade III, *P*=0.079) and they were diagnosed at the same age (58.1 versus 59.3 years, *P*=0.320).

In the subgroup of non-users (N=183), we found that screen-detected breast cancers (N=71) were smaller (18.46 versus 33.01 mm, P<0.001), had a lower NPI (3.63 versus 4.76, P<0.001) and that patients were younger (62.9 versus 69.8 versus 9.001), had more grade I (21.4% versus 5.4%), less grade III lesions (28.6% versus 56.3%, P<0.001) and less lymph node-positive tumours (14.1% versus 43.8%, P<0.001).

Conclusions: HRT-users are younger when diagnosed with an invasive breast cancer, and the lesion is more likely to be screen-detected, with a lower NPI and grade. The effect of HRT is most obvious for breast cancers detected by self-examination: only the palpable, but not the screen-detected breast cancers have better prognostic tumour characteristics in HRT-users. Mode of detection may explain inconsistencies in the literature regarding the effect of HRT on tumour characteristics of operable breast cancers and is an important variable to be taken into account.

References

- Million Women Study Collaborators. Breast cancer and hormone-replacement therapy in the Million Women Study. The Lancet 2003, 362, 419–427.
- Cheblowski RT et al. Influence of estrogen plus progestin on breast cancer and mammography in healthy postmenopausal women: The Women's Health Initiative Randomized Trial. JAMA 2003, 289, 3243–3253.
- Kerlikowske K et al. Prognostic characteristics of breast cancer among postmenopausal hormone users in a screened population. J Clin Oncol 2003, 21, 4314–4321.
- Li CI et al. Relationship between long durations and different regimens of hormone therapy and risk of breast cancer. JAMA 2003, 289, 3254–3263.
- Chen CL et al. Hormone replacement therapy in relation to breast cancer. JAMA 2002, 287, 734–741.
- Bilimoria MM et al. Estrogen replacement therapy and breast cancer: analysis
 of age of onset and tumor characteristics. Ann Surg Oncol 1999, 6, 200–207.
- Bonnier P et al. Impact of menopausal hormone-replacement therapy on clinical and laboratory characteristics of breast cancer. Int J Cancer 1998, 79, 278–282