O-111. FREQUENCY OF BREAST AND OTHER CANCERS AMONG RELATIVES OF MALE BREAST CANCER PATIENTS

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We have previously reported the frequency of BRCA2 gene mutations in a series of male breast cancer patients and shown that carriage of a BRCA2 mutation has no effect on prognosis. Other studies have suggested that BRCA2 mutations are associated not only with an increased risk of male and female breast cancer, but other cancers also e.g. pancreas, ovary, prostate and bladder.

DNA samples from 64 male breast cancer cases were screened for mutations in BRCA2 by use of polymerase chain reaction, heteroduplex analysis, protein truncation testing and sequencing. Living patients were interviewed about family history. An experienced genealogist constructed family pedigrees through access to the Scottish public records of births, deaths and marriages. Ethics committee approval was obtained.

Germline BRCA2 mutations were identified in 12 of the 64 (19%) male breast cancer cases. 8/35 (23%) of female first-degree relatives of mutation carriers had breast cancer compared to 5/132 (4%) female first-degree relatives of non-carriers ($p = 0.0007$, Yates corrected $\chi^2 = 11.48$, 1 d.f.). There were no significant differences between relatives of mutation carriers and non-carriers in terms of the frequencies of pancreatic, ovarian, prostatic, bladder, renal, lung, gastric and colorectal cancers.

Presence of a germline BRCA2 mutation in a proband is associated with a significantly increased frequency of breast cancer in relatives, but any increase in incidence of other cancers is below the limits of detection for a series of this size. This implies that absolute numbers of other cancers will be low within BRCA2 mutation carrying families, therefore it is perhaps questionable that screening for other cancers in relatives of male breast cancer patients is worthwhile.

O-112. THE HISTORY OF BREAST CYSTS IS NOT ASSOCIATED WITH THE DIAGNOSIS OF BREAST CANCER

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Background: The significance of a history of benign cysts to the development of breast cancer is disputed.

Aim: To investigate the relationship of a history of breast cysts to the diagnosis of breast cancer in women attending a symptomatic breast clinic.

Method: Between Jan 1996 and May 1999, 15,205 patients were referred by their GP to the Edinburgh Breast Unit. A structured history was taken; they were specifically asked if they had a cyst previously aspirated or removed surgically. All patients were examined and investigated by a standard protocol. Women over the age of 35 routinely had bilateral mammography. Ultrasound, fine needle aspiration and core biopsy were performed if indicated. Patients were then categorised into 3 groups (normal, benign, malignant). The association between a previous history of benign breast cysts and disease category was tested for statistical significance using a stratified chi-squared tests.

Results: Of the 15,205 patients seen 4,330 (28.5%) were found to be normal, 9,204 (61.2%) had benign disease and 1,571 (10.3%) were found to have malignant disease. The observed numbers of patients with previous cysts in each disease category, compared to the expected number if there was no association is shown in Table 1. There was a substantial excess of normal subjects, with 6% fewer than expected with benign disease and 36% fewer than expected with malignant disease. Analysis within age groups shows similar results.

Diagnostic Group	Previous history of benign cysts	
	Observed No.	Expected No.
Normal	351	275.7
Benign	525	560.5
Malignant	72	111 8

Statified chi squared test. chi squared = 3.96, $p < 0.001$

Conclusion: In women attending a symptomatic breast clinic the history of previous cysts is not associated with the diagnosis of breast cancer.

O-113. THE ZEBRA STUDY: ZOLADEX™ IS AS EFFECTIVE AS CMF IN PRE-/PERIMENOPAUSAL PATIENTS WITH OESTROGEN RECEPTOR POSITIVE, NODE-POSITIVE EARLY BREAST CANCER

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The ZEBRA (Zoladex™ Early Breast Cancer Research Association) study is a large (n = 1640), multicentre, randomized trial initiated in 1990 to compare disease-free survival (DFS), overall survival (OS) and side-effects between Zoladex (goserelin; 3.6 mg every 28 days for 2 years) and cyclophosphamide/methotrexate/5-fluorouracil (CMF; 6 × 28-day cycles) in pre-/perimenopausal patients with node-positive early breast cancer. The efficacy population included 1614 patients: 797 randomized to Zoladex and 817 randomized to CMF. Protocolled subgroup analyses by oestrogen receptor (ER) status showed a highly significant interaction between treatment and ER status ($p = 0.0016$). In ER-positive patients (74% of patients), Zoladex was equivalent to CMF for DFS (HR = 1.01; 95% CI 0.84, 1.20; $p = 0.94$), whereas in ER-negative patients (19% of patients), Zoladex was inferior to CMF for DFS (HR = 1.76; 95% CI 1.27, 2.44; $p = 0.0006$). Over 95% of Zoladex patients achieved amenorrhoea by 6 months compared with approximately 59% of CMF patients. Amenorrhoea was reversible in the majority of Zoladex patients but permanent with CMF: only 23% of Zoladex patients remained amenorrhoeic at 3 years (i.e. 1 year after cessation of Zoladex treatment) compared with 77% of CMF patients. In