Causation

Review: breast cancer is associated with a family history of the disease in first degree relatives

Collaborative Group on Hormonal Factors in Breast Cancer. **Familial breast cancer: collaborative reanalysis of individual data from 52 epidemiological studies including 58 209 women with breast cancer and 101 986 women without the disease.** *Lancet* 2001 Oct 27;358:1389-99.

QUESTION: In women with a family history of breast cancer, how does the pattern of breast cancer in first degree relatives affect the risk of developing the disease?

Data sources

Studies were identified by searching computerised literature databases, reviewing bibliographies of review articles, and contacting experts in the field.

Study selection

Studies were selected if they were cohort or nested case control studies, included ≥ 100 women with incident invasive breast cancer, and information about reproductive or hormonal factors was sought on each woman.

Data extraction

Principal investigators of the included studies were contacted for data on each woman regarding whether any of her first degree female relatives (mother, sisters, or daughters) had been diagnosed with breast cancer and, if so, their age when the diagnosis was made. Data were also collected on the numbers of sisters and daughters of each woman, and the ages of each unaffected first degree female relative.

Main results

52 published and 2 unpublished studies included 58 209 women with breast cancer (median age 52 y) and 101 986 women without breast cancer (median age 53 y). 7496 women (12.9%) with breast cancer and 7438 women (7.3%) without had ≥ 1 first degree female relative with a history of breast cancer. The risk of breast cancer increased with an increasing number of affected relatives (table 1). Age specific relative risks were not affected by race, age at menarche, education, height, weight, or use of contraceptives or hormone replacement therapy. 27 studies provided data on the age that breast cancer was diagnosed in each first degree relative. The risk of breast cancer was higher the younger the relatives were when breast cancer was diagnosed (table 2). The risk of breast cancer was not affected by whether the relative with breast cancer was a mother or a sister, or by the number of sisters a woman had. Too few women had affected daughters to include in the analysis. The estimates of probability that a woman 20 years of age would develop breast cancer by age 50 were 1.7%, 3.7%, and 8.0%, for women with 0, 1, and 2 affected first degree relatives, respectively. The corresponding lifetime probability estimates (ie, age 20-80 y) were 7.8%, 13%, and 21%. The probability estimates for lifetime risk of death were 2.3%, 4.2%, and 7.6%.

Conclusions

Women with first degree relatives with a history of breast cancer are at increased risk for developing the disease. The risk increases with an increasing number of affected

relatives. Most women who develop breast cancer in developed countries do not have a family history of the disease.

Table 1 Relative risk (RR) for breast cancer by number of affected first degree female relatives

Number of first degree relatives	RR for women <50 years (95% CI)	RR for women ≥ 50 years (CI)
1	2.14 (1.92 to 2.38)	1.65 (1.53 to 1.78)
2	3.84 (2.37 to 6.22)	2.61 (2.03 to 3.34)
3	12.05 (1.70 to 85.16)	2.65 (1.29 to 5.46)

Table 2 Relative risk (RR) for breast cancer (BC) by age of affected first degree female relatives

Age at diagnosis of BC in first degree relatives	RR for women <50 years (95% CI)	RR for women ≥ 50 years (CI)
<40 years	13.5 (3.4 to 53.9)	3.9 (1.8 to 8.6)
≥ 40 years	7.8 (2.4 to 25.0)	2.6 (1.8 to 3.7)

COMMENTARY

Although it has long been recognised that a woman's risk of breast cancer is increased if she has a family history of the disease, few individual studies are large enough to provide reliable estimates of the magnitude of this risk. The major strength of this review from the Collaborative Group on Hormonal Factors in Breast Cancer is its size: individual data were pooled from 52 studies of $> 160\ 000$ women to determine the risk of breast cancer in relation to the number of affected first degree female relatives. The important conclusions are that, in industrialised countries, almost 90% of breast cancer patients do not have a family history of breast cancer, and that for women with only 1 affected first degree relative, the increase in risk is modest.

This review is relevant for nurses practising in genetics, oncology, primary care, gynaecology, and in breast screening centres. The tables and figures in the review are of practical value for use in counselling women with a family history of the disease about their breast cancer risk. Currently, these risk estimates are usually derived by applying the Gail¹ and Claus² research models.

Some important limitations should be considered. Because only data on female first degree relatives with breast cancer were collected, these estimates may not apply to families in whom a paternal history of breast, other cancers or features suggestive of a BRCA1 or BRCA2 mutation exist. Few women had 3 first degree relatives with breast cancer, although interestingly, in this group, the estimated lifetime risk of breast cancer (31%) approaches the estimated breast cancer risk in BRCA1 and BRCA2 mutation carriers. In addition, this review did not address the issues of self perceived breast cancer risk or risk counselling strategies. Thus, nurses who are counselling women about their breast cancer risk may need to consult other resources for this information.

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- 1 Benichou J, Gail MH, Mulvihill JJ. *J Clin Oncol* 1996;14:103-10.
- 2 Claus EB, Risch N, Thompson WD. *Cancer* 1994;73:643-51.