Association of family history and other risk factors with breast cancer risk (Sweden)

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Objectives: Women with a family history of breast cancer have an increased risk for the disease. However, the combined impact of family history and other risk factors on breast cancer risk is unclear. We conducted a large epidemiologic study to examine this issue.

Methods. In a population-based case-control study in all of Sweden, 3,345 women aged 50 to 74 years with invasive breast cancer (84 percent of all eligible), and 3,454 controls of similar age (82 percent of all selected) were included. Mailed questionnaires and telephone interviews were used to collect detailed information on potential breast cancer risk factors. Odds ratios (OR) and 95 percent confidence intervals (CI) were estimated through multiple logistic regression.

Results: Women with a history of breast cancer in any first-degree relative had an increased risk of breast cancer compared with those without such a history (OR = 1.96, CI = 1.67-2.30). There was no clear indication of a differential impact of hormonal risk factors (age at menarche, parity, age at first birth, age at menopause, use of exogenous hormones, and weight gain) or body build at age seven among women with and without a positive family history. Yet, benign breast disease and height clearly were related to breast cancer risk in subjects without a family history, whereas seemingly not so in women with a family history. Formal tests for interaction between family history and these factors, however, did not prove statistically significant.

Conclusions: Our findings indicate that established risk factors entail similar associations with breast cancer risk among women with and without family history of the disease. Cancer Causes and Control 1998, 9, 259-267

Keywords: Breast neoplasms, family history, risk factors, Sweden, women.

Introduction

It is well recognized that women with a family history of breast cancer have an increased risk for the disease. However, little is known about the joint effects of inherited genetic susceptibility – as measured by family history – and alterable risk factors for breast cancer. Thus, few preventive actions, except for bilateral mastectomy, can be proposed for high risk women. Assessment of a possible effect modification of family history on the association with other established risk factors is often hampered by low power, and previous studies...
have indeed yielded conflicting results. We had the opportunity to examine this issue in one of the largest population-based case-control studies to date.

Materials and methods

Subjects

This was a population-based case-control study on women aged 50 to 74 years, born in Sweden and resident there between 1 October 1993 and 31 March 1995. We attempted to contact all incident cases of invasive primary breast cancer in this population. Cases were identified through the six Swedish regional cancer registries and were asked to give their written consent to be approached with a mailed questionnaire through their physicians. A total of 3,979 eligible cases were detected, of whom 3,345 (84 percent) participated in the study. Nonparticipation was due to physicians' refusal (because of psychiatric disorder, death, anxiety, or poor physical health in the patients) in four percent of the eligible cases, and patients' refusal (either to be approached at all or to return the questionnaire) or inability to contact the patient in 12 percent. The mean interval from diagnosis to data collection was 4.3 months (standard deviation 1.5 months).

Control women, frequency matched to the expected age distribution of the cases, were randomly selected from a continuously updated Swedish registry which provides National Registration Number, name, address, and place of birth of all people residing in Sweden. Of 4,188 controls selected, 3,454 (82 percent) agreed to participate in the study.

Data collection

Data were obtained by means of an extensive mailed questionnaire requesting information on family history of breast cancer in mother or sister(s) including their age at diagnosis, reproductive and menstrual history, as well as weight at age 18 and one year prior to data collection ('recent weight') and other suggested risk factors for breast cancer. Subjects were also asked to specify which of nine pictograms most resembled their own body build ('somatotype') at age seven (Figure 1). These pictograms have been validated against body mass index (BMI) (wt [kg]/ht [m]²) by others. Further, we found in a population-based validation study of 111 Swedish women (representing 72 percent of a random sample) aged 51 to 66 years that the correlation coefficients between BMI from school records and adult report of somatotype at ages seven and 18 were 0.6 and 0.7, respectively (unpublished data).

Among controls who agreed to participate, 474 (14 percent) failed to return the mailed questionnaire and were subsequently interviewed by telephone. No cases were interviewed in this way since 98 percent of those who had given their consent to receive a questionnaire also returned it. The telephone interview included the most important items in the mailed questionnaire, except family history of breast cancer, weight at age 18, and somatotype. Controls participating through the telephone interview did not differ essentially from other controls with regard to most important risk factors, mean values for the former and latter being 13.8 cf 13.6 years for age at menarche, 49.7 cf 47.6 years for age at menopause, 2.1 cf 2.1 births for parity, and 24.3 cf 24.6 years for age at first birth. Approximately 50 percent of the cases and controls were also contacted by telephone to obtain essential missing information in their mailed responses.

A positive family history of breast cancer was defined, when not specified otherwise, as having either mother or sister(s) affected by the disease. Age at menopause was defined as the age of cessation of natural bleeding or age at bilateral oophorectomy, if one year or more prior to data collection (if later, women were considered premenopausal). Women with hysterectomy, bleeding due to hormone replacement, or missing information were considered postmenopausal if they had reached the age when natural menopause had occurred in 90 percent of the subjects (54 years in current smokers and 55 years in nonsmokers), and otherwise as unknown. Subjects thus classified as postmenopausal were assigned an age at menopause according to their case/control and current smoking status corresponding to the mean age at natural menopause in our data. Benign breast disease (BBD) was defined as having had an operation for a benign breast lump or cyst.

Population for analysis

Women with unknown family history, 83 cases and 526 controls (the higher nonresponse rate in controls being due to the use of telephone administered questionnaires, where this information was not requested), were excluded from all analyses. Further, we excluded the 112