

Induced and spontaneous abortion in relation to risk of breast cancer (United States)

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(Received 3 March 1997; accepted in revised form 11 June 1997)

The relation of induced and spontaneous abortion to the risk of breast cancer is evaluated in a hospital-based case-control interview study conducted in three cities in the United States from 1985 through 1995. Cases were 1,803 women aged 25 to 64 years with newly diagnosed invasive breast cancer; controls were 4,182 women of the same ages admitted for conditions unrelated to reproductive factors. Other breast cancer risk-factors were controlled through multiple logistic regression. The reference for all analyses was women who had never had an abortion, either induced or spontaneous. Among parous women, the relative risk (RR) estimate was 1.1 (95 percent confidence interval [CI] = 0.9-1.5) for induced abortion overall, 1.0 (CI = 0.7-1.4) for abortion before the first birth, and 1.3 (CI = 1.0-1.8) for abortion after at least one birth. Among nulliparous women, the relative risk estimate for induced abortion was 1.3 (CI = 0.9-1.9). There was no trend of increased risk with number of abortions, nor was there consistent evidence of an increased risk in any particular subgroup. Spontaneous abortion was not associated with increased risk of breast cancer, either among nulliparous women or among parous women. These findings provide little support for the hypothesis that induced abortion increases breast cancer risk overall or in particular subgroups. *Cancer Causes and Control* 1997, 8, 841-849

Key words: Abortion, breast carcinoma, risk factors, United States, women.

Introduction

Reproductive factors play a complicated and incompletely understood role in the etiology of breast cancer. Women who give birth to their first child at an early age

appear to have a reduced risk of breast cancer, and nulliparous women appear to have a higher risk than parous women, at least at older ages.¹ Recent work has suggested

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that the risk may increase for a short period after each pregnancy and then decline, eventually resulting in a reduced risk, but this is not established.²⁻⁶

If full-term pregnancies influence the risk of breast cancer, incomplete pregnancies also might have an effect. Pregnant rats treated with chemical carcinogens have been shown to have a lower incidence of breast cancer when the pregnancy is completed than when it is terminated by hysterectomy.⁷ In the animal model, increased hormone secretion causes proliferation of breast cells in early pregnancy; towards the end of a full-term pregnancy there is terminal differentiation, which may reduce susceptibility to carcinogens.^{8,9} Based, in part, on data from studies on rats, it has been postulated that interruption of a pregnancy before differentiation takes place may increase the risk of breast cancer in humans. In epidemiologic studies addressed specifically to elucidation of the roles of induced and spontaneous abortion, the results concerning spontaneous abortion have been predominately null.¹⁰ For induced abortion, the findings have been more mixed¹⁰⁻³¹ and recent results have raised hypotheses about the potential modifying effects of age at abortion, length of gestation, and family history of breast cancer.²³

We previously have reported generally null results on the relation of induced and spontaneous abortion to the risk of breast cancer based on data from our Case-Control Surveillance Study, a hospital-based study of several exposures and diseases.³⁰ Here, we present results from data collected since that report that address the various hypotheses raised in recent studies.

Materials and methods

The Case-Control Surveillance Study has been conducted since 1976 in hospitals in several geographic areas, mostly in the northeastern United States.³² Our nurse-interviewers administered standard interviews to adult patients under age 70 with breast cancer, other malignant disorders, or nonmalignant diseases. Varying proportions of eligible patients with any particular diagnosis were interviewed, depending upon staffing and the priority given to interviewing patients with particular diagnoses. The participation rate of patients approached for an interview was 96 percent, and this rate has been consistent across geographic areas and over time.

Our previous report was based on data collected in Boston (Massachusetts), Baltimore (Maryland), New York City (New York), and Philadelphia (Pennsylvania) from the start of the study through 1984.³⁰ The present report is based on data from patients interviewed from 1985 through 1995 in the latter three cities (there was no further data collection in Boston).

Information was collected on demographic factors,

reproductive history, medical history, use of medications, cigarette and alcohol use, and family history of cancer. Until 1988, reproductive data obtained included age at the end of the first pregnancy, age at first birth, parity, gravidity, number of spontaneous abortions (a pregnancy of less than 24 weeks that ended spontaneously), and number of induced abortions. From mid-1988 onward, questions were asked specifically about the number of induced or spontaneous abortions that preceded the first term-birth, and the age of the woman and length of gestation of all abortions before the first birth. Discharge summaries were obtained for all patients, and pathology reports for all patients with cancer. The pathology reports of all patients who had a discharge diagnosis of breast cancer were reviewed to establish whether the cancer was invasive or *in situ* (including intraductal).

Cases

Potential cases were 1,835 women aged 25 to 64 years who had pathologically confirmed, invasive breast cancer diagnosed within the previous year and no previous or concurrent malignancy other than nonmelanoma skin cancer; not included as cases were 311 women with *in situ* cancer. We excluded 32 cases who had one or more ectopic pregnancies or had missing information on pregnancies. Of the remaining 1,803 cases, 560 were interviewed before the questionnaire was changed in 1988.

Controls

Potential controls were 4,289 women aged 25 to 64 admitted for nonmalignant or malignant conditions judged to be unrelated to reproductive factors. Patients admitted for nonmalignant conditions had not had cancer, and those admitted for malignancies had no previous or concurrent cancer. We excluded 107 controls who had a history of ectopic pregnancy or had missing information on pregnancies, leaving a total of 4,182 controls. The control diagnoses were: traumatic injury (724 patients); infections (405); orthopedic conditions (*e.g.*, disc disorders) (561); gallbladder disease (625); other nonmalignant conditions (1,197); and malignant conditions (cancer of digestive tract other than colon and rectum (196), respiratory tract (195), urinary tract (135), and other (144)). Of the controls, 1,610 were interviewed before the questionnaire was changed in 1988. The prevalence of induced abortion within diagnosis group, standardized to the overall distribution of the controls according to age and geographic area, ranged from nine to 13 percent; the prevalence of spontaneous abortion ranged from 17 to 24 percent (Table 1).

Data analysis

Nulliparous and parous women were analyzed separately in order to minimize the possibility of confounding by