Cancer Causes and Control 1995, 6, 75-82

Abortion and breast cancer risk in seven countries

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(Received 22 August 1994; accepted in revised form 13 October 1994)

Epidemiologic studies have been inconsistent in suggesting an association between abortion and breast cancer risk. Whether the protection provided by a full-term pregnancy also results from a short-term pregnancy or whether a prematurely terminated pregnancy could increase the risk of breast cancer is unclear. Data from a large, international collaborative study were used to evaluate the association between abortions, whether spontaneous or induced, and breast cancer risk. The data from seven countries included 3,958 breast cancer cases and 11,538 hospital controls with information on abortion history obtained through interviews. Compared with nulliparous women with no abortion (baseline), the odds ratios (OR) and 95 percent confidence intervals (CI) were: for nulliparous women with a history of prior abortion, 0.86 (CI=0.68-1.08); for parous women with no history of abortion, 0.63 (CI=0.57-0.69); for parous women with abortion before first birth, 0.82 (CI=0.69-0.97); and, for parous women with abortion only after first birth, 0.70 (CI=0.63-0.79). When restricting analysis to parous women, those with a history of abortion exhibited an elevated OR suggesting a 29 percent risk increase if the incomplete pregnancy occurred before first birth (CI=1.16-1.36) and an 11 percent risk increase for abortion only after first birth (CI=1.02-1.20) compared with women without such history. The associations observed were stronger among the youngest women. These results do not support a large overall association between abortion and breast cancer risk. *Cancer Causes and Control* 1995, 6, 75-82

Key words: Abortion, breast cancer, international comparison, miscarriage, pregnancy.

Introduction

The possibility that abortion, whether spontaneous or induced, increases the risk of breast cancer was raised by Pike *et al*[1] in a case-control study of women 32 years of age or younger at time of diagnosis. Other studies have been inconsistent, with some suggesting an increased risk, but others showing little association or even implying an inverse association.[2-34] Differences in populations studied, study design, and analytical approaches may explain some variability of findings, but it is also possible that discrepancies are due partly to the choice of the reference (baseline) group.

In several case-control studies,[2-16] no important difference was found in the odds of breast cancer among women who had abortions and those who did not. In the international collaborative effort led by MacMahon in the late 1960s and early 1970s, a trend towards higher number of abortions among breast cancer cases was seen in some countries[18-20] but not in others.[2-5] In some other studies in which data on abortions were collected retrospectively positive associations were found in some comparisons.[17,21-27] In case-control studies conducted in San Francisco (California, United States),[28] the United Kingdom,[29] and Portugal,[30] inverse associations were observed.

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The relation between abortion and breast cancer has been examined in four cohort studies. In a retrospective cohort of 3,315 women,[31] a threefold increase in risk was observed for women who had a spontaneous abortion before the first full-term pregnancy and subsequently gave birth, relative to women who also had a livebirth but no prior abortion. Such association was not found, and even was reversed slightly, among women for whom it could not be determined whether the abortion preceded or followed their first livebirth. The number of breast cancer cases observed in this study was small. Kvåle *et al*[32] found a modest, but not significant, risk reduction among 63,090 Norwegian women who reported at least one abortion. This reduction was greatest in women aged 50 years and older. An inverse association between induced abortion in women before age 30 and breast cancer rates also was seen in a Swedish study utilizing an abortion registry.[33] The low risk was restricted to women who were parous at the time of the index abortion (relative risk [RR]=0.58, 95 percent [CI]=0.38-0.84), while the risk of nulliparous women did not seem affected. No relationship was found in the Iowa Women's Health Study comprising 37,105 women.[34]

The rationale for considering an association between abortion and breast cancer risk derives from the established influence of pregnancy on the risk of breast cancer. A full-term pregnancy increases the short-term risk of breast cancer, possibly due to the growth-enhancing properties of pregnancy estrogens, but decreases the long-term risk, possibly by inducing terminal differentiation of the susceptible mammary tissue.[35-41] It is not known whether and to what extent a prematurely terminated pregnancy might share one or both of the dual effects of a full-term pregnancy. Data from experimental animals are limited and not altogether clear, but they seem to indicate that the potential for terminal differentiation is substantially lower for a pregnancy terminated by abortion compared with a full-term pregnancy.[42] Russo *et al*[43] have suggested that complete differentiation of the breast cells conveyed by a full-term pregnancy has to be achieved to provide protection. During the first three months of pregnancy, estrogens are substantially higher than those found in non-pregnant women, but considerably lower than those noted during the later stages of pregnancy. It is plausible that the effect of pregnancy estrogen on breast cancer risk depends on the duration of elevation as well as the actual level of increase.

We have analyzed the data from the large, international, collaborative case-control study to evaluate the role, if any, of abortions in modulating breast cancer risk. This is the largest dataset utilized so far for the evaluation of the relation between abortion and breast cancer risk.

Materials and methods

Data obtained in seven countries as part of an international collaborative study with similar protocols at all study sites were pooled for the present analysis.[44] The study covered areas with low (Taipei, Taiwan; Tokyo, Japan), intermediate (Athens, Greece; São Paulo, Brazil; Slovenia, then part of Yugoslavia), and high (Boston, US; Glamorgan, Wales, UK) incidence of breast cancer. An attempt was made to identify all residents of the defined population having a diagnosis of breast cancer established for the first time during the specified time period. Except in Tokyo and São Paulo, where the cases represented about 50 percent and 70 percent of all incident cases, respectively, most female residents of the study areas hospitalized for a first diagnosis of breast cancer during the study period were included.

A histologic specimen was obtained from each patient and sent to the coordinating center for review by a single pathologist. Information on the variables of interest was obtained through interviews during the time of hospitalization conducted by trained personnel. The same interview form, translated as required, was used in all centers.

For each breast cancer patient interviewed, three eligible patients who occupied the hospital beds closest to that of the index case were chosen as controls and interviewed. Generally, the same interviewer would interview all members of a 'set' consisting of one breast cancer patient and three controls. To be eligible, a control had to be a resident of the study area, never have had cancer of the breast, and be 35 years of age and over (except when the index case was under 35, in which event controls were age-matched within two years). In some instances, three eligible controls could not be obtained for each cancer case.

The number of miscarriages and abortions was indirectly calculated. The woman was asked by the interviewer to give detailed information on every pregnancy including month and year of birth, whether it was a livebirth or stillbirth, and how many months the pregnancy lasted. Pregnancies lasting less than five months were classified as miscarriages or induced abortions. At the time of data collection, induced abortions were legal in Slovenia and Japan and widely practiced in Athens and São Paulo, although not formally legalized.

The interviewers were asked to give an opinion on the validity of the information obtained at each interview.