

Pregnancy after breast cancer: population based study

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EDITORIAL by Banks and Reeves

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ABSTRACT

Objectives To identify women who survived breast cancer and subsequently conceived and to determine the rate of pregnancy (proportion), management, outcome of the cancer, and outcome of the first subsequent pregnancy.

Design Population based descriptive study with cases identified from the Western Australian data linkage system and validated by review of medical charts. Supplementary data obtained from hospital and clinician records.

Setting Western Australia, 1982-2003.

Participants Women aged <45 with a diagnosis of breast cancer who subsequently conceived.

Main outcome measures Pregnancy outcome and rate, survival, time from diagnosis to pregnancy.

Results Sixty two (54%) women with a diagnosis of breast cancer who subsequently conceived did so less than two years after their diagnosis: 29 of them had an abortion, 27 had a live birth, and six miscarried. Within a proportional hazards regression model subsequent pregnancy was associated with improved overall survival (hazard ratio 0.59, 95% confidence interval 0.37 to 0.95). When the model was stratified by time from diagnosis subsequent pregnancy was associated with improved overall survival in women who waited at least 24 months to conceive (0.48, 0.27 to 0.83) and a non-significant protective effect was seen for women who waited at least six months to become pregnant.

Conclusions Our study does not support the current medical advice given to premenopausal women with a diagnosis of breast cancer to wait two years before attempting to conceive. This recommendation may be valid for women who are receiving treatment or have systemic disease at diagnosis, but for women with localised disease early conception, six months after completing treatment, is unlikely to reduce survival.

INTRODUCTION

Women who have received a diagnosis of breast cancer are often advised to wait at least two years after treatment before they attempt to conceive. There are no published data to suggest that postponing conception will alter the outcome of the cancer or pregnancy. The two year wait is suggested as a guide and is based on anecdotal evidence. The delay is primarily to deter women who may develop early recurrence and to allow the completion of adjuvant therapies.

Previous reports suggest that women who survive breast cancer and subsequently conceive have at

least equivalent, if not better, survival than similar women matched for age and stage of cancer who do not subsequently conceive.¹⁻⁷ This may be due to selection bias called the “healthy mother” effect; women with a diagnosis of breast cancer who subsequently conceive are a self selecting group of women with better prognosis.⁸

We identified women who survived breast cancer and subsequently conceived in the Western Australian population in 1982-2003 and determined the pregnancy rate (proportion), management, and outcomes of the breast cancer and first subsequent pregnancy.

METHODS

We used the Western Australian data linkage system⁹ to identify women with breast cancer who conceived at least once after their diagnosis of cancer (see bmj.com for details).

We identified potential cases in two stages. Firstly, the linkage system identified women who were discharged from hospital with an international classification of diseases (ICD) code or a cancer or death registration for breast cancer from 1 January 1982 to 31 December 2000. Age at diagnosis was restricted to 15-44 years. Secondly, we used ICD diagnostic or procedure codes, or both, to identify women with a pregnancy subsequent to their diagnosis of breast cancer but before 31 December 2003. The outcome of the pregnancy could be abortion, miscarriage, ectopic, stillbirth, or live birth.

We used pathology reports in the Western Australian cancer registry and hospital and clinician records to validate cases. A researcher reviewed these records to obtain additional data including demographics, breast symptoms, method of diagnosis, management details, characteristics of the tumour, management and outcome of subsequent pregnancy (including dates of last menstrual period, gestational age, and time from diagnosis of breast cancer to the estimated date of the last menstrual period), and overall survival. A case was confirmed when we identified and validated a pregnancy after the first diagnosis of breast cancer.

Statistical analysis

We used descriptive analysis and included frequency, cross tabulations, χ^2 tests and Fisher's exact tests where applicable, and Kaplan Meier. We used Cox's proportional hazards regression model with a time dependent covariate. We designated the date of the

Table 1 | Time from diagnosis of breast cancer to subsequent pregnancy and outcome of pregnancy. Figures are numbers of pregnancies (percentages)

Time to pregnancy	Full term	Miscarriage	Termination	Total
0-2 years*	27 (43)	6 (10)	29 (47)	62
0-6 months†	6 (30)	4 (20)	10 (50)	20
7-24 months†	21 (50)	2 (5)	19 (45)	42
>2 years	39 (64)	9 (15)	13 (21)	61
Total	66 (54)	15 (12)	42 (34)	123

* $\chi^2=8.870$, 2df, $P=0.012$ Fisher's exact test—comparison for all pregnancy outcomes when conception before or after 24 months from diagnosis.

† $\chi^2=7.738$, 2df, $P=0.021$ Fisher's exact test, when conceptions <6 months after diagnosis excluded.

first pathological diagnosis as the date of diagnosis and the date of the woman's last menstrual period as the date the pregnancy commenced. Overall survival was calculated and defined as the time from the date of diagnosis to the date of death or 31 December 2004. See bmj.com for details.

RESULTS

In 1982-2000, 2539 women aged 15-44 in Western Australia had a pathologically confirmed diagnosis of breast cancer. Of these, 123 (5%) had at least one pregnancy after their diagnosis and before 31 December 2004. The median age of the women who conceived after diagnosis was 31 (interquartile range 28-35). The median age at first subsequent pregnancy was 35 (31-38). The women who had a live birth after diagnosis were generally older than women in the general population who had a live birth (see bmj.com).

In total, 175 subsequent pregnancies were confirmed in the 123 women; 45 (37%) women had more than one subsequent pregnancy. Sixty six (54%) women had a live birth (table 1). Three women successfully underwent in vitro fertilisation treatment to conceive after their diagnosis; at follow-up they were alive and without recurrence. The median time from diagnosis to first subsequent pregnancy was 23 months (interquartile range 11-42).

Sixty two (50%) women conceived within two years of their diagnosis. Abortion was more common when conception occurred within two years of diagnosis ($P=0.012$) and proportionally more abortions occurred in the first six months after breast cancer was diagnosed and while the woman was undergoing active treatment (50% v 45%) (table 1). There was still a statistical difference in outcome of pregnancy between women who delayed conception two

years and those who conceived within two years ($P=0.021$), even when we excluded women who conceived within six months of diagnosis (that is, during most adjuvant treatment) from the analysis. See bmj.com for stage and characteristics of tumours.

Most women had breast conserving surgery ($n=70$, 57%). Only seven (6%) women were confirmed to have started hormone therapy (tamoxifen) and at least one conceived. She stopped when the pregnancy was discovered and had a full term live birth. Three women underwent ovarian tissue preservation before treatment but conceived naturally after adjuvant chemotherapy. Fifty women (41%) had chemotherapy and 26 (52%) of these did not wait two years to become pregnant.

One hundred and four (85%) women who had a pregnancy after cancer were reported to be alive with a median follow-up of 128 months (interquartile range 80-182). All the women who died in this study died from causes related to breast cancer. Disease recurred in 48 (39%) women, with a median overall time without recurrence of 42 months (interquartile range 20-75). The five year overall survival was 92% (95% confidence interval 87% to 97%), and 10 year overall survival was 86% (80% to 93%). Five year and ten year survival from first subsequent pregnancy was 87% (81% to 93%) and 85% (78% to 91%), respectively.

The Cox's proportional hazard regression model with subsequent pregnancy as a time dependent covariate showed that subsequent pregnancy improved overall survival (table 2). Subsequent pregnancy improved overall survival in those women who waited 24 months to become pregnant and had a non-significant protective effect for all women who waited at least six months to become pregnant (table 3).

DISCUSSION

Currently premenopausal women with a diagnosis of breast cancer are advised to wait two years before attempting to conceive. Our study does not support this, although the recommendation may be valid for women who are receiving treatment or have systemic disease at diagnosis. For women with localised disease, early conception after completion of their breast cancer management is unlikely to adversely affect their survival.

Pregnancy rate

In our study the proportion of women who survived breast cancer and who conceived was lower than the proportion seen in the general population. Women with a diagnosis of breast cancer were more likely to have a live birth at a later age than seen in the general population because of the cancer treatment. The two year delay recommended after the end of treatment would further reduce the number of women who would conceive. We could not identify which women remained fertile after the diagnosis and therefore the pregnancy rate is a conservative estimate. The 123 (5%) women who did conceive was similar to the number in a Danish population based study, but some

Table 2 | Cox's proportional hazards model for survival in women with breast cancer with time dependent variable

	β coefficient	P value	Hazard ratio (95% CI)
Age at diagnosis	-0.03	<0.001	0.97 (0.96 to 0.99)
Lymph node positive	0.96	<0.001	2.61 (2.17 to 3.13)
Tumour size (mm):			
<20			1.0
20-50	-0.49	<0.001	0.61 (0.50 to 0.75)
>50	0.05	0.592	1.05 (0.87 to 1.27)
Unknown	0.40	0.026	1.49 (1.05 to 2.10)
Subsequent pregnancy	-0.53	0.030	0.59 (0.37 to 0.95)

Table 3 | Cox's proportional hazards model* for survival in women with breast cancer with time dependent variable stratified by time from diagnosis

Time to subsequent pregnancy (months)	β coefficient	P value	Hazard ratio (95% CI)
<6	0.79	0.579	2.20 (0.14 to 35.42)
6-24	-0.80	0.135	0.45 (0.16 to 1.28)
>24	-0.74	0.009	0.48 (0.27 to 0.83)

*Each stratified model adjusted for age, lymph node status, and tumour size.

of the women in our study may have conceived after our cut-off date (31 December 2004).¹⁰

Pregnancy outcome

Anecdotal evidence suggests that there were four main reasons why women conceived within two years: they conceived between diagnosis and adjuvant treatment, when they were not aware that they would need chemotherapy and radiotherapy; advice on contraception was not given or not understood at the time of diagnosis; failure of a contraceptive method; and the desire to have a child above anything else. It is concerning that women are becoming pregnant during adjuvant treatment.

Fertility

The use of adjuvant chemotherapy did not affect the outcome of pregnancy in women who became pregnant at least six months after their diagnosis; more of these women had live births than had an abortion or miscarried. These outcomes were in similar proportions to those reported previously.^{11 12} Hormone therapy was not available to women early in the study period, but even when it became available and was recommended many women chose not to take it.

To ask women to delay conception for two years after a diagnosis of breast cancer may allow the identification of those who relapse early and have a poor prognosis. For women with a good prognosis, however, adjuvant chemotherapy regimens may induce early menopause and at the least reduce ovarian reserve. This has considerable clinical implications for the advice given to younger women diagnosed with breast cancer who have good prognostic markers and want the opportunity to conceive after treatment.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Women who survive breast cancer and who conceive >24 months after diagnosis have similar or better survival than other women with breast cancer

Women are currently advised to wait at least two years after treatment for breast cancer before conception

Women with a diagnosis of breast cancer who have adjuvant chemotherapy may reduce their chance of later conceiving

WHAT THIS STUDY ADDS

For women with localised disease and good prognosis conception six months after treatment is unlikely to reduce survival

Pregnancy is unlikely to compromise the survival prospects for women treated for breast cancer who have tumours with good prognosis

Survival

Overall survival at five (92%) and ten (86%) years was better for women who subsequently conceived than has been reported in similar cohorts.^{2 4 11 13 14} This increased survival, while in part due to the "healthy mother" effect, could also be related to the improved management in breast cancer and increased survival seen for all women in Western Australia diagnosed during the time period.

When we accounted for time to pregnancy, improved survival was significant only for women who waited at least 24 months to conceive. Others have reported the same.¹¹ In our study there was a definite protective effect for women who waited at least six months to conceive. We would expect that this result would become significant if more women conceived 6-24 months after treatment. The results reflect the clinical recommendation that women delay pregnancy for two years after diagnosis and suggest that women who have a good prognosis need not wait two years to become pregnant.

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