Original Study

# Breast Cancer Outcomes After Diagnosis of Hormone-positive Breast Cancer and Subsequent Pregnancy in the Tamoxifen Era

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## Abstract

**Pregnancy after the diagnosis of breast cancer is an important survivorship issue. We conducted a retrospective analysis that included 32 premenopausal women with a diagnosis of estrogen receptor-positive breast cancer and subsequent pregnancy and an age- and stage-matched control cohort without subsequent pregnancy. The results of the present study did not demonstrate poorer disease-free survival in women who became pregnant within 5 years after their cancer diagnosis.**

**Background:** Counseling patients regarding the risk of future pregnancy on hormone receptor-positive breast cancer outcomes is difficult because of the minimal data and understanding of pregnancy on the breast environment. **Patients and Methods:** The present retrospective analysis included 32 premenopausal women with a diagnosis of estrogen receptor-positive breast cancer from 2000 to 2010 and subsequent pregnancy within 5 years. The control cohort included 29 women matched for age and stage of breast cancer who had not become pregnant. **Results:** No statistically significant difference was found in age, diagnosis, stage, grade, or HER2 status between the 2 groups. Of the 32 women in the pregnancy cohort and 29 women in the control cohort, 19 (63%) and 23 (82%) had received endocrine therapy ($P = .25$). The mean length of endocrine therapy was 42.3 months (range, 0-120 months) in the control cohort and 20.9 months (range, 0-72 months) in the pregnancy cohort ($P = .008$). Four women (14%) in the control cohort experienced breast cancer recurrence compared with 8 women (26%) in the pregnancy cohort ($P = .34$). The 5-year disease-free survival rate was 92% (95% confidence interval, 81%-100%) in the control cohort compared with 84% (95% CI, 72%-97%) in the pregnancy cohort. The difference was not statistically significant ($P = .69$). **Conclusion:** The results of the present study did not demonstrate poorer disease-free survival for premenopausal women with estrogen receptor-positive breast cancer who became pregnant within 5 years of diagnosis. Our study is unique because all included patients had estrogen receptor-positive disease and were offered adjuvant hormonal therapy. Further prospective investigation will be beneficial to patients and physicians as they discuss pregnancy as a key survivorship issue.

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## Introduction

Breast cancer is the most commonly diagnosed malignancy in women aged 30 to 45 years, and this age group accounts for 10.8% of newly diagnosed breast cancer cases annually in the United States.[1] With the trend of women delaying pregnancy and childbirth until later in life, fertility preservation after a diagnosis of breast cancer and future pregnancy is a growing concern.[2] Although great advancements have been made in fertility preservation for cancer patients, many women and their physicians are hesitant to consider or recommend pregnancy with a history of hormone receptor-positive breast cancer, and many patients are recommended against future pregnancy.[3] Although the potential for negative consequences resulting from the increased hormonal milieu associated with pregnancy is of high theoretical concern to physicians, no data have suggested that pregnancy after a diagnosis of breast cancer is associated with a greater rate of recurrence or death. Furthermore, limited data are available on the risk of breast cancer

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recurrence after pregnancy since tamoxifen became the standard of care for adjuvant therapy for hormone receptor-positive breast cancer and significantly improved outcomes. We investigated the breast cancer outcomes of premenopausal women diagnosed with hormone receptor-positive breast cancer at our cancer center during the tamoxifen era, who subsequently became pregnant within 5 years after their breast cancer diagnosis.

## Patients and Methods

The patients included in the pregnancy cohort were premenopausal women, aged ≥ 18 years with a diagnosis of breast cancer. The histologic types included ductal carcinoma in situ, invasive ductal carcinoma, and invasive lobular carcinoma that was stage 0 to IIIA (Tis-T3N0-N2). The tumor had to have been estrogen receptor-positive (> 1%). Also, all included women had to have been considered for adjuvant tamoxifen therapy. The women in the pregnancy cohort must have achieved a pregnancy (including miscarriage) within 5 years after the diagnosis of breast cancer.

The patients in the control (no pregnancy) cohort were also premenopausal women, aged ≥ 18 years, with a diagnosis of stage 0 to IIIA, estrogen receptor-positive breast cancer. Using the Northwestern Medicine Enterprise Data Warehouse, the control group was matched by age and stage to the pregnancy cohort. However, these patients had not achieved a pregnancy within 5 years after the diagnosis of breast cancer. All included women had been considered for adjuvant tamoxifen therapy.

A query was conducted in the Northwestern Medicine Enterprise Data Warehouse to identify female patients aged ≥ 18 years at the diagnosis of breast cancer (International Classification Diagnosis [ICD] code, 174.X) or ductal carcinoma in situ (ICD code, 233.0) and a subsequent diagnosis of pregnancy (ICD, 9th revision, code, V22.2 or alternative pregnancy code) within 5 years after the breast cancer diagnosis who had been seen at Northwestern University Hospital from 2000 to 2010. A review of the patients' electronic medical records was conducted to identify patients who met the inclusion criteria and obtain data on the included patients regarding diagnosis, tumor characteristics and staging, treatment history, pregnancy history, and outcomes. Disease recurrence included local and metastatic disease.

For the statistical analysis, categorical variables were summarized using frequencies and percentages and compared between groups using Fisher's exact test. Continuous variables were summarized using the mean, standard deviation, median, and range and compared between groups using the Wilcoxon rank sum test. Disease-free survival (DFS) was summarized using Kaplan-Meier curves and compared between groups using the log-rank test.

## Results

Of the 61 patients, 32 were included in the pregnancy cohort and 29 in the control (no pregnancy) cohort. No statistically significant difference was found in age, diagnosis, stage, tumor grade, or HER2 status between the 2 groups. More tumors in the control (no pregnancy) cohort had progesterone receptor-positive disease, 27 (93%) compared with 21 (70%) in the pregnancy cohort ($P$ = .042). The patient and tumor characteristics are listed in Table 1.

The surgical interventions were similar between the cohorts, with a trend toward contralateral prophylactic mastectomy in the control (no pregnancy) cohort. However, the difference was not statistically significant. Adjuvant therapy was also similar between the 2 groups, including those who received adjuvant endocrine therapy and radiation therapy. The recurrence score, as analyzed using the 21-gene reverse transcription-polymerase chain reaction assay, and chemotherapy details were not available for most patients and, therefore, were not included in the present review. Of the 32 women included in the pregnancy cohort, 19 (63%) received endocrine therapy. In the control (no pregnancy) cohort, 23 of the 29 women (82%) received endocrine therapy ($P$ = .25). Women were considered to have received endocrine therapy (tamoxifen) even if initiation of treatment was delayed, interrupted, or discontinued because of pregnancy. The treatment interventions are summarized in Table 2. The mean duration of endocrine therapy was significantly longer in the control (no pregnancy) cohort at 42.3 months (range, 0-120 months) compared with that in the pregnancy cohort (mean, 20.9 months; range, 0-72 months; $P$ = .008).

The follow-up duration was shorter in the control (no pregnancy) cohort (mean, 78 months; range, 23-168 months) than in the pregnancy cohort (mean, 110 months; range 57-185 months; $P$ = .005). No statistically significant difference was found in the incidence of breast cancer recurrence between the women who became pregnant within 5 years after the diagnosis of breast cancer and those who did not. Four women (14%) in the control (no pregnancy) cohort experienced breast cancer recurrence compared with 8 women (26%) in the pregnancy cohort ($P$ = .34). In the pregnancy cohort, 19 of 32 women took adjuvant tamoxifen (63%). Of these women, 7 took adjuvant tamoxifen before the subsequent pregnancy and did not resume after pregnancy, 6 women delayed

**Table 1 Patient and Tumor Characteristics**

| Characteristic | Control Group (No Pregnancy; n = 29) | Pregnancy Group (n = 32) | *P* Value |
|---|---|---|---|
| Diagnosis | | | .99 |
| DCIS | 7 (24) | 8 (25) | |
| Invasive breast cancer | 22 (76) | 24 (75) | |
| Stage | | | .84 |
| 0 | 7 (24) | 8 (26) | |
| IA | 11 (38) | 9 (29) | |
| IB | 0 (0) | 1 (3) | |
| IIA | 5 (17) | 5 (16) | |
| IIB | 2 (7) | 5 (16) | |
| IIIA | 4 (14) | 3 (10) | |
| Grade | | | .74 |
| 1 | 5 (18) | 6 (21) | |
| 2 | 12 (43) | 9 (31) | |
| 3 | 11 (39) | 14 (48) | |
| PR positive | 27 (93) | 21 (70) | .042 |
| HER2 positive | 5 (22) | 4 (14) | .71 |
| Age (y) at diagnosis | 36.1 (26-46) | 34.2 (28-46) | .12 |
| BRCA mutated[a] | 1/17 (6) | 4/16 (25) | .17 |

Data presented as n (%) or mean (range).
Abbreviations: DCIS = ductal carcinoma in situ; PR = progesterone receptor.
[a]Unavailable for 28 patients.