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The Impact of Pregnancy on Breast Cancer Outcomes in Women ≤35 Years

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Abstract

BACKGROUND—Some evidence suggests that women with pregnancy-associated breast cancers (PABC) have a worse outcome compared with historical controls. However, young age is a worse prognostic factor independently, and women with PABC tend to be young. The purpose of the current study was to compare locoregional recurrence (LRR), distant metastases (DM), and overall survival (OS) in young patients with PABC and non-PABC.

METHODS—Data for 668 breast cancers in 652 patients aged ≤35 years were retrospectively reviewed. One hundred four breast cancers (15.6%) were pregnancy-associated; 51 cancers developed during pregnancy and 53 within 1 year after pregnancy.

RESULTS—The median follow-up for all living patients was 114 months. Patients who developed PABC had more advanced T classification, N classification, and stage group (all $P < .04$) compared with patients with non-PABC. Patients with PABC had no statistically significant differences in 10-year rates of LRR (23.4% vs 19.2%; $P = .47$), DM (45.1% vs 38.9%; $P = .40$), or OS (64.6% vs 64.8%; $P = .60$) compared with patients with non-PABC. For those patients who developed breast cancer during pregnancy, any treatment intervention during pregnancy provided a trend toward improved OS compared with delaying evaluation and treatment until after delivery (78.7% vs 44.7%; $P = .068$).

CONCLUSIONS—Young patients with PABC had no statistically significant differences in LRR, DM, or OS compared with those with non-PABC; however, pregnancy contributed to a delay in breast cancer diagnosis, evaluation, and treatment. Primary care and reproductive

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physicians should be aggressive in the workup of breast symptoms in the pregnant population to expedite diagnosis and allow multi-disciplinary treatment.

Keywords

breast cancer; breast-conserving therapy; pregnancy; pregnancy-associated breast cancer; young age

Pregnancy associated breast cancer (PABC), defined as breast cancer that develops either during or within 1 year after pregnancy, presents both a diagnostic and a therapeutic dilemma. PABC is relatively rare, with an estimated 0.2% to 3.8% of pregnancies being complicated by breast cancer,[1] and approximately 10% of breast cancer patients aged <40 years developing the disease during pregnancy.2 However, as maternal age at the time of pregnancy continues to increase, from a median of 26.0 years in 1982 to 27.4 years in 2002,3 the incidence of PABC can be expected to increase. As a result, optimal diagnostic strategies and treatment approaches are of paramount importance.

Prior studies of PABC have been limited by the rarity of this clinical entity. Previous reports have suggested that PABC tends to be more advanced than non-PABC.[4–6] Furthermore, some studies have suggested that the relatively poor outcome of these patients may be because of this aspect of their disease, rather than the pregnancy itself, and that pregnant patients may not have a worse prognosis when age and stage are taken into account.[7,8] However, all of these studies have been hindered by relatively small sample sizes, heterogeneous treatment techniques that have evolved over time, and limited controls. More recently, prospective studies have begun to address the issue of optimal management of PABC to maximize outcome for both the patient and the fetus.[9]

Given the complexity of issues involved with the treatment of PABC, the purpose of this retrospective study was to compare the rates of locoregional recurrence (LRR), distant metastases (DM), and overall survival (OS) in young patients (aged ≤35 years) who developed PABC versus young patients with non-PABC.

METHODS AND MATERIALS

Patient Selection

We retrospectively reviewed the records of women diagnosed with breast cancer at age ≤35 years; this cohort included 668 individual breast cancers in 652 women. Patients were grouped based on the relation between their breast cancer and pregnancy; PABC was defined as breast cancer that developed either 1) during or 2) within 1 year after pregnancy. Non-PABC was defined as breast cancer that met neither of these definitions. Patients who clearly developed the symptoms of their breast cancer during pregnancy but whose diagnostic workup was delayed until after delivery were considered as having developed cancer “during” pregnancy; this is in contrast to patients who developed symptoms clearly after delivery. All patients were treated between 1973 and 2006 at the University of Texas M. D. Anderson Cancer Center. Patients with a primary diagnosis of inflammatory breast cancer (n = 29), ductal carcinoma in situ (n = 5), breast sarcoma (n = 1), and unknown or unevaluable primary cancer (n = 13) were excluded from analysis, as were those who developed metastatic disease within 6 months of diagnosis (n = 26) and those who did not receive a definitive surgery (n = 7). For this analysis, all patients were restaged according to the 2002 American Joint Committee on Cancer staging guidelines.[10] For patients treated with neoadjuvant chemotherapy, the most advanced stage (initial clinical and/or pathologic stage) was used; for patients who were not treated with neoadjuvant chemotherapy, the pathologic stage was used.

Standard Treatment

All patients received definitive locoregional treatment with breast-conserving therapy, mastectomy alone, or mastectomy with adjuvant radiation. The ultimate decisions regarding treatment strategy, pregnancy management, and the use of both chemotherapy and hormonal therapy were based on the clinical staging, physician discretion, and patient choice. Because treatment modalities evolved during the course of this study, recommended treatment did differ based on the date of diagnosis. As chemotherapy became a key component of multimodality treatment, it was increasingly integrated into our treatment approach; chemotherapy was given both neoadjuvantly and/or adjuvantly based on the physician's discretion. Chemotherapy was also administered after completion of the first gestational trimester for some patients who were treated on a prospective institutional review board (IRB)-approved protocol.[9]

Statistical Analysis

The frequencies of all pathologic and clinical factors between the groups of patients were compared using the chi-square statistic. Endpoints were calculated as the interval of time between pathologic diagnosis of the primary cancer and the event of interest. Local recurrence was a disease recurrence in the ipsilateral breast, chest wall, or overlying skin. LRR was the first ipsilateral local or regional lymph node recurrence (including axillary, supraclavicular, infraclavicular, or internal mammary lymph node beds). Any other site of recurrence was coded as a DM. All LRRs were considered independent events regardless of their relation to DM in time. The 10-year actuarial rates of LRR, DM, and OS were calculated using the Kaplan-Meier statistic, and comparisons between groups were calculated using the log-rank test. All *P* values were 2-sided, and only *P* values ≤.05 were considered to be statistically significant. Cox regression and multivariable analysis were not performed because of the small patient numbers in each patient group.

RESULTS

Patient Characteristics

Of the 668 breast cancers included in this study, 104 (15.6%) were considered PABC; 51 cancers developed during pregnancy, and 53 developed within 1 year after pregnancy. The median follow-up for all living patients was 114 months (range, 7 months–411 months). The median follow-up for all patients was 91 months (range, 2 months–411 months); the median follow-up for patients with PABC was 95.5 months, and that for patients with non-PABC was 91 months. The median age of all patients was 33 years (range, 16 years–35 years); the median age for patients with PABC was 33 years, and that for patients with non-PABC was 32 years. Table 1 shows the patient, tumor, and treatment characteristics for the entire study population.

As shown in Table 1, patients with PABC had more advanced T classification, N classification, AJCC stage, and stage group compared with those with non-PABC (all $P < .04$). In addition, patients with PABC were more likely to be treated with mastectomy and radiation compared with non-PABC patients ($P = .04$). There were no statistically significant differences noted in the groups with regard to age, race, laterality of the cancer, family history of breast or ovarian cancer, decade of treatment, histology, nuclear grade, lymphovascular space invasion (LVSI), estrogen receptor positivity, use of chemotherapy, or use of hormonal therapy; there was a borderline difference in progesterone receptor positivity, but this was largely because of patients for whom this variable was unknown.

As shown in Table 2, there were few differences noted between patients with PABC who developed breast cancer during pregnancy compared with 1 year after pregnancy. Those

patients diagnosed during pregnancy had a higher proportion of tumors with LVSI present than those diagnosed within 1 year after pregnancy (43.1% vs 22.6%; *P* = .03). There were no other statistically significant differences noted between these 2 groups of patients with PABC.

Overall Outcome in Patients Aged ≤35 Years

For all cases of breast cancer diagnosed in patients aged ≤35 years (n = 668), the Kaplan-Meier 10-year actuarial LRR was 19.8%, DM was 39.9%, and OS was 64.6%. Previous analysis of this entire population demonstrated that treatment with mastectomy alone (compared with either mastectomy with adjuvant radiation or breast-conserving therapy) (*P* = .05), increasing N classification (*P* = .004), and increasing American Joint Committee on Cancer (AJCC) stage (*P* = .02) were predictors of LRR.[11]

Impact of Pregnancy on Outcome

To investigate the impact of pregnancy on breast cancer outcome, 10-year actuarial rates of LRR, DM, and OS were compared between those patients with PABC versus non-PABC. There was no statistically significant difference noted with regard to the 10-year actuarial LRR rates between young patients with PABC and those with non-PABC (23.4% vs 19.2%; *P* = .47) (Fig. 1 *Left*) (Table 3). There were also no statistically significant differences between patients with PABC and those with non-PABC with regard to the 10-year actuarial rates of DM (45.1% vs 38.9%; *P* = .40) and OS (64.6% vs 64.8%; *P* = .60) (Figs. 1 *Center* and *Right*) (Table 3).

To further delineate the role of pregnancy, those patients with PABC were divided into those who developed breast cancer during pregnancy (n = 51) and those who developed it within 1 year after pregnancy (n = 53). Comparing these 2 groups, there were no statistically significant differences in the 10-year actuarial rates of LRR (15.0% vs 30.0%; *P* = .17), DM (43.2% vs 46.1%; *P* = .89), or OS (62.6% vs 64.9%; *P* = .52) (Fig. 2) (Table 3).

Impact of Treatment on PABC

Of the 51 patients who developed breast cancer during pregnancy, 25 received no treatment during their pregnancies, and 26 received some sort of treatment (Table 4). Of those 25 who received no treatment, 22 patients (88%) had symptoms that were not evaluated (no pathologic diagnosis or workup during pregnancy), and the remaining 3 patients (12%) had a pathologic diagnosis but were instructed to delay treatment until after delivery. Of those 26 who received some sort of treatment, this varied between chemotherapy, locoregional surgery, and therapeutic abortion followed by immediate intervention. Given the small sample sizes, the overall groups (treatment vs no treatment) were compared to determine whether the administration of any treatment intervention affected outcome. There was a trend toward improved OS for those patients who received any treatment compared with those who did not (78.7% vs 44.7%; *P* = .068) (Fig. 3) (Table 4). These differences, however, reflect the outcome of a small number of patients. There were no statistically significant differences in LRR (12.9% vs 17.2%; *P* = .70) or DM (38.5% vs 48.3%; *P* = .51).

DISCUSSION

In this retrospective study of young patients (aged ≤35 years) with operable breast cancers, those with PABC have a similar outcome with regard to LRR, DM, and OS as those with non-PABC. One striking finding is that patients with PABC presented with more advanced T classification, N classification, and AJCC stage than similar patients with non-PABC. This suggests that the largest risk for patients with PABC is the delay of diagnosis of their disease.

PABC is a relatively rare entity that presents unique challenges for both diagnosis and management. Prior reports have suggested that approximately 10% of breast cancers diagnosed in patients aged ≤40 years were diagnosed during pregnancy.[2] In this study, 15.6% of breast cancers diagnosed in patients aged ≤35 years were considered pregnancy-associated; overall, 7.6% were diagnosed during pregnancy and 7.9% within 1 year after delivery. Although the rate of this study is generally consistent with published reports, the increase over the expected rate (15.6% vs 10%) may be attributable to the finding that the M. D. Anderson Cancer Center has conducted the only prospective trial for PABC in North America.[9] Our data suggest that the patients who develop PABC may not be promptly diagnosed and evaluated. Prioritization of the pregnancy and other psychosocial issues may play a role in this. In addition, normal variations in breast density and potential benign conditions that are more common during pregnancy, including engorgement and mastitis, can both mimic and mask the symptoms of breast cancer.12،13 Although the current study does not address the issue of false-negative results in screening these women, it does suggest that women who are pregnant or within 1 year of delivery who develop breast cancer are diagnosed with more advanced stage disease than those who have not had an associated pregnancy. This suggests that physicians who care for these patients should be more aggressive in the workup and diagnostic evaluation of breast symptoms in this population. Although routine mammography is not indicated given the potential radiation exposure to the fetus, use of mammography with appropriate fetal shielding has been safely integrated into the evaluation of patients on prospective trials of PABC.9 In addition, ultrasound is an appropriate diagnostic study and may provide valuable information with no risk to the unborn child.

Once diagnosed, young patients (aged ≤35 years) with PABC have similar outcomes as young patients with non-PABC, both overall and stage-by-stage, which are relatively poor compared with historical breast cancer series comprising all age groups. This suggests that the poorer outcomes are largely a result of the young age of the patients and not the pregnancy itself. This is consistent with prior reports in the literature. Zemlickis et al reviewed the cases of 118 women diagnosed with breast cancer during pregnancy and 269 nonpregnant controls, and they found that the women who presented while pregnant had more advanced disease but no difference in outcome, with a 10-year OS of 40% for patients with PABC and 48% for those with non-PABC.[5] Other retrospective studies demonstrated similar results with regard to overall survival. Ezzat et al reported a 7-year overall survival rate of 57% for patients with PABC versus 61% for patients with non-PABC.8 Bonnier et al reported a 5-year overall survival of 61% for PABC versus 75% for non-PABC.4 Middleton et al evaluated the histopathology of 39 patients with PABC and found that the pathologic findings correlated with those described in young cohorts, having poor prognostic and histologic features; there were no unique histopathologic features identified within the PABC group specifically.14 The current study did find that patients with PABC who were diagnosed during pregnancy had a statistically significant increased rate of LVSI compared with patients diagnosed in the 1 year after delivery; however, their outcomes were statistically similar. In aggregate, these data suggest that patients with PABC do not have an inferior outcome when diagnosed either during pregnancy or within 1 year after delivery; nonetheless, significant improvements need to be made in the management of all breast cancers in this group of young patients.

Limitations in our understanding of PABC, from the perspective of optimal management of both the mother and fetus, are currently being addressed with prospective IRB-approved trials. The outcome of pregnant patients and their fetuses treated with systemic chemotherapy including 5-fluorouracil, doxorubicin, and cyclophosphamide is currently being addressed with a large, single-arm, institutional study at the M. D. Anderson Cancer Center. Current data suggest that this regimen is well tolerated, with minimal toxicity to the

unborn child, and with maternal outcomes consistent with published reports.[9] Although these data are preliminary, they suggest that women with PABC can be well managed with neoadjuvant chemotherapy and that termination is not necessary to optimize the outcomes of either mother or child. Further follow-up is needed to characterize any potential long-term sequelae to this strategy for both the mothers and children, including comprehensive medical assessments as the children enter their reproductive years.

The similar outcomes for young women with PABC and those with non-PABC demonstrated in this study are intriguing; however, there are inherent limitations to the current investigation. Given that the data were collected retrospectively, there are limitations in the information available as well as potential biases that may have contributed to treatment decisions and impacted outcomes. We have attempted to minimize these differences by excluding patients with inflammatory breast cancer (n = 29), who are treated at our institution with an aggressive treatment schema that is different from the standard therapy, and likely represent a cohort of patients with different underlying biology.[15–17] It should be noted that clinical difficulty in discerning skin involvement in pregnant patients secondary to breast engorgement or pregnancy-related breast skin changes would be expected to lead to an over-representation of false-positive T4 staging. These data are difficult to discern retrospectively. However, this bias, if present, would make the differences in stage at presentation less significant rather than more significant and further support the conclusions as reported. In addition, because the scope of this review extends before routine metastatic screening with computed tomography, we have excluded those patients (n = 26) who developed metastatic disease within 6 months of diagnosis, because we believe that these likely represent patients with underappreciated metastatic disease at presentation. For the remaining patient population, we have attempted to elucidate any differences by comparing the patient groups and indicated discrepancies when they are statistically significant. Furthermore, this study extends for several decades during which treatment philosophies, techniques, and technologies have evolved. We have analyzed outcome by decade and found no statistically significant differences; although treatment regimens may have changed, there is no evidence that this historical evolution has contributed to our observations and conclusions. Although our data are strengthened by a large patient population, these findings should be viewed as hypothesis-generating. The lack of a statistically significant correlation between the diagnosis of PABC and a worse outcome does not necessarily preclude a true association. Furthermore, it is difficult to determine whether the concurrent pregnancy, with its hormonal and physiologic effects, influences the stage and aggressivity of the underlying malignancy. Our study does, however, provide hypothesis-generating data that among young women with breast cancers of similar stage and treatment, differing predominantly by pregnancy association, outcomes are statistically similar; notably, these outcomes are consistently worse than those for older women with similar disease and treatment. Additional studies with increased power will be necessary to fully elucidate the interaction of gestational hormonal influences with breast cancer pathogenesis and to attempt to separate these from interactions that occur secondary to young age itself.

Our current study highlights the importance of adequate diagnosis and treatment in the management of PABC. Pregnancy itself does not impart a worse prognosis; however, pregnancy does mask symptoms and hinder diagnosis. The education of patients and primary care physicians that breast symptoms during and immediately after pregnancy should be fully investigated will help hasten diagnosis and maximize treatment. Of those patients who were diagnosed during pregnancy, there is a trend toward improved outcome with any treatment given. Those patients in whom diagnosis was delayed or treatment deferred until after delivery had an inferior survival compared with those who received immediate diagnosis followed by chemotherapy, surgery, or therapeutic abortion (followed

by immediate treatment). Overall, breast cancer in young patients (aged ≤35 years) is an aggressive disease; improvement in comprehensive multidisciplinary management is needed in all patients, but especially in those patients whose cancers are associated with pregnancy. Balancing the health of mother and child is also paramount; new evidence suggests that both can be prioritized and successful outcomes managed for both.

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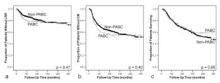

FIGURE 1.
Kaplan-Meier curves for (*Left*) locoregional recurrence (LRR)-free survival, (*Center*) distant metastasis (DM)-free survival, and (*Right*) overall survival for patients aged ≤35 years who were diagnosed with pregnancy-associated breast cancer (PABC) are shown in gray versus the same curves for nonpregnancy-associated breast cancer (non-PABC), as shown in black.

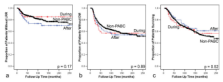

FIGURE 2.

Kaplan-Meier curves are shown for (*Left*) locoregional recurrence (LRR)-free survival, (*Center*) distant metastasis (DM)-free survival, and (*Right*) overall survival for patients aged ≤35 years who were diagnosed with pregnancy-associated breast cancer (PABC) during pregnancy (“During”) (red) and within 1 year of delivery (“After”) (blue), and non-PABC (black). The *P* values reflect comparisons between the 2 groups of patients with PABC (During vs After).

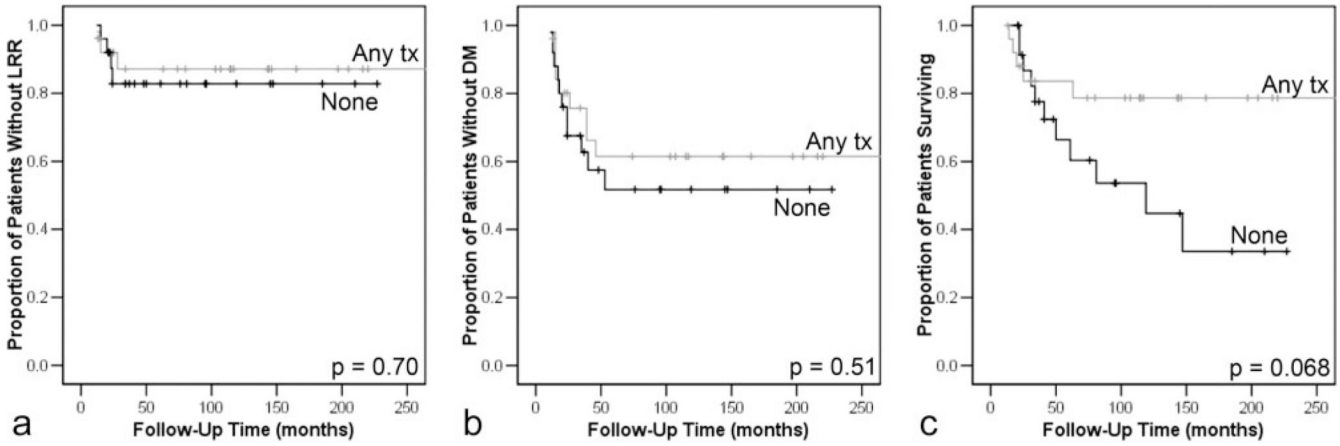

FIGURE 3.

Kaplan-Meier curves are shown for (*Left*) locoregional recurrence (LRR)-free survival, (*Center*) distant metastasis (DM)-free survival, and (*Right*) overall survival for patients aged ≤35 years who were diagnosed with breast cancer during pregnancy based on receipt of treatment ("Any tx") (gray) compared with no treatment ("None") (black).

Table 1

Patient and Tumor Characteristics for the Entire Population and by Overall Pregnancy Association

	Total (%)	No. Non-PABC (%)	No. PABC (%)	*P**
All cancers	668 (100)	564 (84.4)	104 (15.6)	
Age at diagnosis, y				**.45**
≤19	2 (0.3)	2 (0.4)	0 (0)	
20–24	18 (2.7)	15 (2.7)	3 (2.9)	
25–29	137 (20.5)	110 (19.5)	27 (26.0)	
30–35	511 (76.5)	437 (77.5)	74 (71.2)	
Race				**.29**
White/Caucasian	414 (62.0)	347 (61.5)	67 (64.4)	
Black/African American	99 (14.8)	89 (15.8)	10 (9.6)	
Hispanic	135 (20.2)	110 (19.5)	25 (24.0)	
Other	20 (3.0)	18 (3.2)	2 (1.9)	
Family history				**.24**
Negative	395 (59.1)	328 (58.2)	67 (64.4)	
Positive distant	176 (26.3)	148 (26.2)	28 (26.9)	
Positive first-degree relative	88 (13.2)	79 (14.0)	9 (8.7)	
Unknown	9 (1.3)	9 (1.6)	0 (0)	
Decade of treatment				**.24**
1973–1979	42 (6.3)	39 (6.9)	3 (2.9)	
1980–1989	154 (23.1)	134 (23.8)	20 (19.2)	
1990–1999	357 (53.4)	294 (52.1)	63 (60.6)	
2000–2006	115 (17.2)	97 (17.2)	18 (17.3)	
T classification				**.004**
T1	201 (30.1)	181 (32.1)	20 (19.2)	
T2	273 (40.9)	233 (41.3)	40 (38.5)	
T3	123 (8.4)	95 (16.8)	28 (26.9)	
T4	57 (8.5)	42 (7.4)	15 (14.4)	
TX	14 (2.1)	13 (2.3)	1 (1.0)	
N classification				**.03**
N0	222 (33.2)	191 (33.9)	31 (29.8)	
N1	233 (34.9)	203 (36.0)	30 (28.8)	
N2	129 (19.3)	98 (17.4)	31 (29.8)	
N3	84 (12.5)	72 (12.8)	12 (11.5)	
AJCC stage				**.03**
I	101 (15.1)	92 (16.3)	9 (8.7)	
IIA	164 (24.6)	142 (25.2)	22 (21.2)	
IIB	132 (19.8)	114 (20.2)	18 (17.3)	
IIIA	138 (20.7)	107 (19.0)	31 (29.8)	
IIIB	40 (6.0)	29 (5.1)	11 (10.6)	
IIIC	84 (12.6)	72 (12.8)	12 (11.5)	

	Total (%)	No. Non-PABC (%)	No. PABC (%)	*P**
Unknown (TX, N0-2)	9 (1.3)	8 (1.4)	1 (1.0)	
Stage group				**.03**
I	101 (15.1)	92 (16.3)	9 (8.7)	
II	296 (44.4)	256 (45.4)	41 (39.4)	
III	262 (39.2)	208 (36.9)	53 (51.0)	
Unknown (TX, N0-2)	9 (1.3)	8 (1.4)	1 (1.0)	
Histology				**.88**
Invasive ductal	622 (93.1)	525 (93.1)	97 (93.3)	
Invasive lobular	14 (2.1)	11 (2.0)	3 (2.9)	
Invasive mixed	14 (2.1)	12 (2.1)	2 (1.9)	
Unknown/other	18 (2.6)	16 (2.8)	2 (1.9)	
Nuclear grade				**.86**
Low	9 (1.3)	7 (1.2)	2 (1.9)	
Intermediate	207 (31.0)	175 (31.0)	32 (30.8)	
High	389 (58.2)	327 (58.0)	62 (59.6)	
Unknown	63 (9.4)	55 (9.8)	8 (7.7)	
Final margin status				**.83**
Negative	564 (84.4)	479 (84.9)	85 (81.7)	
Close (<2 mm)	52 (7.8)	43 (7.6)	9 (8.7)	
Positive	23 (3.4)	19 (3.4)	4 (3.8)	
Unknown	29 (4.3)	23 (4.1)	6 (5.8)	
ER status				**.19**
Negative	274 (41.0)	223 (39.5)	51 (49.0)	
Positive	268 (40.1)	232 (41.1)	36 (34.6)	
Unknown	126 (18.9)	109 (19.3)	17 (16.3)	
PR status				**.05**
Negative	283 (42.4)	228 (40.4)	55 (52.9)	
Positive	216 (32.3)	186 (33.0)	30 (28.8)	
Unknown	169 (25.3)	150 (26.6)	19 (18.3)	
LVSI				**.93**
Absent	447 (66.9)	377 (66.8)	70 (67.3)	
Present	221 (33.1)	187 (33.2)	34 (32.7)	
Chemotherapy				**.19**
No	69 (10.3)	62 (11.0)	7 (6.7)	
Yes	599 (89.7)	502 (89.0)	97 (93.3)	
Hormone therapy				**.39**
No	504 (75.4)	429 (76.1)	75 (72.1)	
Yes	164 (24.6)	135 (23.9)	29 (27.9)	
Locoregional treatment				**.04**
Breast-conserving therapy	197 (29.5)	171 (30.3)	26 (25.0)	
Mastectomy alone	237 (35.5)	207 (36.7)	30 (28.8)	
Mastectomy and radiation	234 (35.0)	186 (33.0)	48 (46.2)	

PABC indicates pregnancy-associated breast cancer; AJCC, American Joint Committee on Cancer; ER, estrogen receptor; PR, progesterone receptor; LVSI, lymphovascular space invasion.

*P represents comparison of the 2 treatment groups (PABC vs non-PABC).

Table 2

Patient and Tumor Characteristics by Detailed Pregnancy Association

	No. During Pregnancy (%)	No. Within 1 Year (%)	*P*
All patients	51 (7.6)	53 (7.9)	
Age at diagnosis, y			**.23**
≤19	0 (0)	0 (0)	
20–24	1 (2.0)	2 (3.8)	
25–29	17 (33.3)	10 (18.9)	
30–35	33 (64.7)	41 (77.4)	
Race			**.86**
White/Caucasian	31 (60.8)	36 (67.9)	
Black/African American	6 (11.8)	4 (7.5)	
Hispanic	13 (25.5)	12 (22.6)	
Other	1 (2.0)	1 (1.9)	
Family history			**.40**
Negative	30 (58.8)	37 (69.8)	
Positive distant	15 (29.4)	13 (24.5)	
Positive first-degree relative	6 (11.8)	3 (5.7)	
Unknown	0 (0)	0 (0)	
Decade of treatment			**.66**
1973–1979	1 (2.0)	2 (3.8)	
1980–1989	10 (19.6)	10 (18.9)	
1990–1999	29 (56.9)	34 (64.2)	
2000–2006	11 (21.6)	7 (13.2)	
T classification			**.12**
T1	7 (13.7)	13 (24.5)	
T2	17 (33.3)	23 (43.4)	
T3	19 (37.3)	9 (17.0)	
T4	8 (15.7)	7 (13.2)	
TX	0 (0)	1 (2.3)	
N classification			**.35**
N0	14 (27.5)	17 (32.1)	
N1	14 (27.5)	16 (30.2)	
N2	19 (37.3)	12 (22.6)	
N3	4 (7.8)	8 (15.1)	
AJCC stage			**.09**
I	3 (5.9)	6 (11.3)	
IIA	10 (19.6)	12 (22.6)	
IIB	6 (11.8)	12 (22.6)	
IIIA	22 (43.1)	9 (17.0)	
IIIB	6 (11.8)	5 (9.4)	
IIIC	4 (7.8)	8 (15.1)	

	No. During Pregnancy (%)	No. Within 1 Year (%)	*P*
Unknown (TX, N0-2)	0 (0)	1 (1.9)	
Stage group			**.10**
I	3 (5.9)	6 (11.3)	
II	16 (31.4)	25 (47.2)	
III	32 (62.7)	21 (39.6)	
Unknown (TX, N0-2)	0 (0)	1 (1.9)	
Histology			**.51**
Invasive ductal	48 (94.1)	49 (92.5)	
Invasive lobular	2 (3.9)	1 (1.9)	
Invasive mixed	0 (0)	2 (3.8)	
Unknown/other	1 (2.0)	1 (1.9)	
Nuclear grade			**.65**
Low	1 (2.0)	1 (1.9)	
Intermediate	13 (25.5)	19 (35.8)	
High	32 (62.7)	30 (56.6)	
Unknown	5 (9.8)	3 (5.7)	
Final margin status			**.07**
Negative	37 (72.5)	48 (90.6)	
Close (<2 mm)	6 (11.8)	3 (5.7)	
Positive	4 (7.8)	0 (0)	
Unknown	4 (7.8)	2 (3.8)	
ER status			**.49**
Negative	28 (54.9)	23 (43.4)	
Positive	16 (31.4)	20 (37.7)	
Unknown	7 (13.7)	10 (18.9)	
PR status			**.80**
Negative	28 (54.9)	27 (50.9)	
Positive	15 (29.4)	15 (28.3)	
Unknown	8 (15.7)	11 (20.8)	
LVSI			**.03**
Absent	29 (56.9)	41 (77.4)	
Present	22 (43.1)	12 (22.6)	
Chemotherapy			**.06**
No	1 (2.0)	6 (11.3)	
Yes	50 (98.0)	47 (88.7)	
Hormone therapy			**.59**
No	38 (74.5)	32 (60.4)	
Yes	13 (25.5)	16 (30.2)	
Locoregional treatment			**.47**
Breast-conserving therapy	13 (25.5)	13 (24.5)	
Mastectomy alone	12 (23.5)	18 (34.0)	
Mastectomy and radiation	26 (51.0)	22 (41.5)	

AJCC indicates American Joint Committee on Cancer; ER, estrogen receptor; PR, progesterone receptor; LVSI, lymphovascular space invasion.

Table 3

Ten-year Actuarial Rates of LRR, DM, and OS According to Pregnancy Association

	No. of Patients	LRR, %	*P*	DM, %	*P*	OS, %	*P*
No association (non-PABC)	564	19.2	.47	38.9	.40	64.8	.60
PABC (all)	104	23.4		45.1		64.6	
During pregnancy	51	15.0	.17	43.2	.89	62.6	.52
Within 1 y of delivery	53	30.0		46.1		64.9	

LRR indicates locoregional recurrence; DM, distant metastases; OS, overall survival; PABC, pregnancy-associated breast cancer.

Table 4

Ten-year Actuarial Rates of LRR, DM, and OS for Patients Developing Breast Cancer During Pregnancy by Treatment Approach

	No. of Patients	LRR (%)	*P*	DM (%)	*P*	OS (%)	*P*
No treatment	25	17.2	.70	48.3	.51	44.7	.068
Any treatment	26	12.9		38.5		78.7	
Chemotherapy	13	9.1		35.3		72.9	
Local surgery	7	14.3		14.3		85.7	
Therapeutic abortion	6	20.0		66.7		83.3	

LRR indicates locoregional recurrence; DM, distant metastases; OS, overall survival.