Postoperative Complications following Lumpectomy and Mastectomy in Women with Pregnancy Associated Breast Cancer

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Abstract

Purpose: This study aimed to delineate postoperative complications following lumpectomy and mastectomy in women with pregnancy associated breast cancer (PABC).

Methods: This is a single institution retrospective study of 74 patients with PABC treated with lumpectomy (n=28) or mastectomy (n=46). Patient demographics, presentation, tumor characteristics, staging, genetic testing, and postoperative complications were recorded.

Results: PABC was diagnosed in 74 patients; 28 (37.8%) were diagnosed with PABC during pregnancy (PABC-P) and 46 patients (62.2%) were diagnosed with postpartum PABC within the first 12 months after delivery (PABC-PP). The overall clinical stage distribution at diagnosis was: Stage 0, 6.9%; I, 18.1%; II, 47.2%; III, 22.2%; and IV, 5.6%, with no significant difference between PABC-P and PABC-PP (p=0.18). There was no significant difference in the rate of lumpectomy (25.0% vs 23.9%, p=0.92), mastectomy (75.0% vs 76.1%, p=0.92), sentinel lymph node biopsy (39.3% vs 52.2%, p=0.28), axillary dissection (14.3% vs 4.3%, p=0.19), or rate of immediate reconstruction (42.9% vs 65.7%, p = 0.094) performed in patients with PABC-P and PABC-PP, respectively. Contralateral prophylactic surgery was performed in 43.2% of patients (39.3% PABC-P vs 47.5% PABC-PP, p=0.59). Most (79.9%) patients did not experience any postoperative complications, regardless of whether they underwent lumpectomy or mastectomy (83.3% vs 78.6%, p=0.99) or if they had PABC-P or PABC-PP (89.3% vs 73.9%, p=0.11). There was a statistically significant difference in the rate of complications between PABC-P patients undergoing mastectomy with immediate reconstruction (n=0/9, 0%) as compared to the PABC-PP patients (n=9, 39%; p=0.035). Seroma was the most commonly observed complication after both lumpectomy and mastectomy (n=3 vs n=5, p=0.39).

Conclusions: There was no increased risk of postoperative complications in women with PABC treated with lumpectomy as compared to mastectomy. There is an increased risk of postoperative complications in patients with PABC-PP treated with mastectomy and immediate reconstruction.

Introduction

Pregnancy associated breast cancer (PABC), which includes cancer diagnoses both during pregnancy (PABC-P) & in the first year postpartum (PABC-PP), is the second most common malignancy in pregnancy, affecting approximately 1 in 3000 women[1]. Treatment for PABC includes chemotherapy when indicated and surgical resection [2, 3]. Breast surgery can be performed at any stage of pregnancy. Classically women with PABC-P have been offered mastectomy, but lumpectomy can also be considered if radiation is deferred until the postpartum period[4].

The incidence of post-operative surgical complications in women with PABC is poorly studied. The largest study reports on a total of 67 patients treated prior to 2009, of whom 20 patients underwent lumpectomy and 47 patients underwent mastectomy without immediate reconstruction for PABC. The authors reported a 10% postoperative complication rate in the patients undergoing lumpectomy and 8.5% in those undergoing mastectomy without reconstruction [5]. The reported complication rate appears to be similar in patients with PABC who were treated with mastectomy and immediate reconstruction, ranging from 0–10% [6, 7].

The incidence of post-operative complications in the setting of PABC in more contemporary cohorts is unclear. The primary aim of this study is to identify the incidence of complications following breast surgery for pregnancy associated breast cancer.

Methods

This is an IRB approved retrospective study involving patients treated at Cleveland Clinic between January 1, 2000 to December 31, 2020. Eligible patients were identified from a pool of all patients with a pregnancy episode during 2000 to 2020 by searching for relevant ICD and CPT codes during the pregnancy episode and the year following the pregnancy episode. ICD diagnosis codes queried included breast cancer, unspecified (ICD 9: 174.9, ICD 10: C50.919). CPT codes queried included partial mastectomy with or without axillary lymphadenectomy (19301, 19302), simple mastectomy (19303), subcutaneous mastectomy (19303), radical mastectomy (19305, 19306), and modified radical mastectomy (19307). Patients were considered eligible for the study if they had a biopsy proven malignancy during their pregnancy or within one year of delivery. Patients with Stage IV disease who underwent surgery as part of their treatment based on multidisciplinary team discussion and disease response to primary systemic therapy were included in this study.

Patients that did not have a pregnancy episode created within the electronic medical record were identified by searching a database of all breast cancer patients under 50 within the Cleveland Clinic enterprise from Jan 1, 2009 – December 31, 2020. This database was queried in four ways. First, eligible patients were identified by searching the database for cesarean section (CPT 59514) and diagnosis of breast cancer, unspecified (ICD 9: 174.9, ICD 10: C50.919) within 365 days of the procedure date. Next, the diagnosis codes for supervision of normal pregnancy (ICD 9: V22 ICD 10: Z34.9), pregnant (ICD 9: V22.2, ICD 10: Z33), and induction of labor (ICD 9: 73.4) were queried and subsequently searched for a breast cancer diagnosis code within 365 days of the procedure date. Finally, operative reports of breast procedures coded under CPT codes 19301, 19302, 19303, 19305, 19306, and 19307 were searched for the word "pregnancy." Patients were considered eligible for the study if they had a biopsy proven malignancy during their pregnancy or within 12 months of delivery and underwent breast surgery at Cleveland Clinic as part of their treatment. Patient demographics, pregnancy, tumor biology and treatment details were collected. The electronic medical record (EMR) was reviewed to determine the chief complaint for patients presenting with PABC. Patients were offered genetic testing and results were reviewed. Decision for lumpectomy or mastectomy was based on multidisciplinary discussion, patient preference and timing of surgery in relation to delivery for PABC-P patients. Nodal management was determined based on tumor biology and multidisciplinary discussion. All patients undergoing mastectomy were offered a plastic/reconstructive surgery consult. Adjuvant therapy was based on tumor stage, biology and trimester for those women with PABC-P. Thirty day surgical complications collected included seroma, nipple necrosis, skin flap necrosis, milk duct fistula, surgical site infection, wound dehiscence, hematoma, organ space surgical site infection, pneumonia, urinary tract infection, sepsis, septic shock, failure to wean, reintubation, intraoperative anesthetic complications, deep vein thrombosis, pulmonary embolism, acute renal failure, progressive renal insufficiency, peripheral nerve deficit, cerebral vascular accident, coma, myocardial infection, cardiac arrest, transfusion, and death.

Statistical analysis

Approximately normally-distributed continuous measures were summarized using means and standard deviations and compared using Wilcoxon Rank Sum tests. Categorical factors were summarized using frequencies and percentages and were compared using Pearson’s chi-square tests or Fisher’s Exact tests. All p values were two-sided, with 0.05 as level of statistical significance and 95% CI. Statistical analysis was performed using SAS software version 9.4 (SAS Institute Inc., Cary NC).

Results

We identified 74 patients diagnosed with PABC with a mean age of 34.5. There were 28 patients (37.8%) with PABC-P and 46 patients (62.2%) with PABC-PP diagnosed within the first 12 months after delivery. When comparing with PABC-P and PABC-PP, there was no significant difference in age at diagnosis (Mean ± SD: PABC-P: 34.4 ± 3.4 vs PABC-PP: 34.5 ± 4.0, p = 0.87), BMI (Median IQR: PABC-P: 27.8 [22.8, 31.6] vs PABC-PP: 26.1 [22.5, 31.0], p = 0.52), or medical comorbidities (Table 1).

The majority of patients presented complaining of a palpable mass (86.5%, n = 64), pain (17.6%, n = 13), or erythema (6.8%, n = 5) (Table 1). Other common presenting complaints included decreased milk production (6.5% of PABC-PP, n = 3), change in bra size (2.7%, n = 2), presumed abscess (2.7%, n = 2), and nipple retraction (2.7%, n = 2). The patient's mass was initially palpated by their physician 4.1% of the time (n = 3). Patients experienced symptoms for a median of 1 month [IQR: 0.25, 4.0] prior to presentation (Table 1). The overall clinical stage distribution at diagnosis was: Stage 0, 6.9%; I, 18.1%; II, 47.2%; III, 22.2%; and IV, 5.6%. There was no significant difference in clinical stage at presentation in PABC-P and PABC-PP (p = 0.18) (Table 2).

Patients with PABC-P were diagnosed at a median gestational age of 27.1 [IQR: 9.8, 32.6] weeks, underwent surgery at 34.2 [IQR: 15.9, 52.6] weeks, and delivered at 37.4 [IQR: 35.6, 39.0] weeks, most commonly via vaginal delivery (52.7%) (Table 1). Patients diagnosed postpartum were diagnosed on average 16.3 weeks postpartum.

Overall, 90.5% of patients elected to undergo genetic testing (Table 1). There was no significant difference in the rate of genetic testing between patients with PABC-P and PABC-PP (82.1% vs 95.7%, p = 0.097). Among those tested, the majority (52.2%, n = 35) of patients overall did not have any identifiable mutation, but PABC-PP patients were less likely to have a pathogenic mutation (63.6%, n = 28) than PABC-P patients (30.4%, n = 7; p = 0.01). BRCA1 mutations were observed in 26.1% (n = 6) of PABC-P patients and 22.7% (n = 10) of PABC-PP patients (p = 0.76). BRCA2 mutations were observed in 4.3% (n = 1) of PABC-P patients and 4.5% (n = 2) of PABC-PP patients (P = 0.76). One BARD1 mutation was observed (PABC-P: 4.3% vs PABC-PP: 0%, p = 0.34). Of note, 16.4% (n = 11) of patients, including 30.4% (n = 7) of PABC-P patients and 9.1% (n = 4) of PABC-PP patients (p = 0.04), were found to have a VUS (Table 1).

Regarding tumor biology, most (68.1%, n = 49) patients had histologic grade 3 disease (PABC-P: 75.0%, n = 21 vs PABC-PP: 63.6%, n = 28; p = 0.62) (Table 2). Triple negative (Estrogen receptor (ER) negative, progesterone receptor (PR) negative, Her 2 negative) tumors were seen in 29.7% (n = 22) of patients (PABC-P: 32.1%, n = 9 vs PABC-PP: 28.3%, n = 13; p = 0.72). Hormone receptor positive (+) tumors (ER + and/or PR+) were seen in 58.1% (n = 43) of women (PABC-P: 57.1%, n = 16 vs PABC-PP: 58.7%, n = 27; p = 0.90). Her2 + tumors were seen in 25.7% (n = 19) of patients (PABC-P: 25.0%, n = 7 vs PABC-PP: 26.1%, n = 12; p = 0.92) (Table 2).

Overall, 45.9% of patients received neoadjuvant chemotherapy, and while patients with PABC-PP were more likely to receive neoadjuvant chemotherapy the finding was not statistically significant (32.1%, n = 9 vs 54.3%, n = 25; p = 0.06) (Table 3). There was no significant difference in the time to the start of neoadjuvant chemotherapy (median 20.0 days [IQR: 16.0, 36.0] vs 18.0 days [IQR: 14.0, 29.0] days, p = 0.27) or in the number of cycles of neoadjuvant chemotherapy (median 6 cycles [IQR: 5.0, 8.0] vs 6 cycles [IQR: 4.0, 8.0], p = 0.82) for patients with PABC-P and PABC-PP, respectively. In patients treated with surgery initially, the median time from diagnosis to surgery was longer for patients with PABC-PP compare to PABC-P but was not statistically significant (35.0 days [IQR: 19.0, 160.5] vs 89.0 days [IQR: 33.0, 158.0] days, p = 0.17).

Postoperative pathology showed similar rates of pathologic complete response following neoadjuvant chemotherapy (33.3%, n = 3 vs 40.0%, n = 10; p = 0.99) for PABC-P and PABC-PP (Table 2).

Overall 18 patients (24.3%) were treated with lumpectomy and 56 patients (75.7%) with mastectomy. There was no significant difference in the rate of lumpectomy (25.0%, n = 7 vs 23.9%, n = 11; p = 0.92) or mastectomy (75.0%, n = 21 vs 76.1%, n = 35; p = 0.92) performed in patients with PABC-P and PABC-PP, respectively (Table 3). The most common type of mastectomy performed was a modified radical mastectomy (31.1%, n = 23) followed by skin sparing mastectomy (21.6%, n = 15), simple mastectomy (12.2%, n = 9), and nipple sparing mastectomy (10.8%, n = 8), with no significant difference in procedure performed regardless of whether patients were diagnosed during pregnancy or postpartum. Sentinel lymph node biopsy (39.3%, n = 11 vs 52.2%, n = 24; p = 0.28) and axillary dissection (14.3%, n = 4 vs 4.3%, n = 2; p = 0.19) were also statistically as likely to be performed in patients with PABC-P and PABC-PP, respectively. The rate of immediate breast reconstruction did not differ for PABC-P and PABC-PP patients (42.9%, n = 9 vs 65.7%, n = 23; p = 0.094). Of those undergoing immediate reconstruction, the majority had a tissue expander placed (PABC-P: 38.1%, n = 8 vs PABC-PP: 51.4%, n = 18; p = 0.31). A small number of patients underwent immediate direct to implant reconstruction (5.4%, n = 3), immediate autologous reconstruction (5.4%, n = 3), or delayed reconstruction (5.4%, n = 3). Contralateral prophylactic mastectomy was performed at the time of the initial surgery in 43.2% (n = 32) of patients (PABC-P: 39.3%, n = 11 vs PABC-PP: 45.7%, n = 21; p = 0.59). Patients with a known pathogenic mutation were more likely to undergo contralateral prophylactic surgery at the time of initial management as compared to patients with a VUS or no identified mutation (81.3% vs 33.3%, p < 0.001). Margin re-excision was required and performed in 12.2% (n = 9) of patients (PABC-P: 10.7%, n = 3 vs PABC-PP: 13.0%, n = 6; p = 0.99) (Table 3).

The majority (79.7%, n = 59) of patients did not experience any postoperative complications, regardless of whether they underwent lumpectomy or mastectomy (lumpectomy: 83.3%, n = 15 vs mastectomy: 78.6%, n = 44; p = 0.99) or if they were diagnosed and treated during pregnancy or postpartum (PABC-P: 89.3%, n = 25 vs PABC-PP: 73.9%, n = 34; p = 0.11) (Table 4). Notably, 60% (n = 9) of the total observed complications (n = 15) were seen in PABC-PP patients who had mastectomy with immediate reconstruction. There was a statistically significant difference in the rate of complications between PABC-P patients undergoing mastectomy with immediate reconstruction (n = 0, 0%) as compared to the PABC-PP patients (n = 9, 39%; p = 0.035).

Seroma was the most commonly observed complication after both lumpectomy and mastectomy (lumpectomy: 16.7%, n = 3 vs mastectomy: 8.9%, n = 5; p = 0.39) (Table 4). Superficial and deep surgical site infections were observed in 5.4% (n = 3) and 1.8% (n = 1) of patients undergoing mastectomy, respectively; no infections were observed following lumpectomy (Table 4). One patient was diagnosed with partial nipple necrosis which was managed conservatively (Table 4). Two patients, one of whom was treated with lumpectomy and the other who was treated with mastectomy with reconstruction, experienced wound dehiscence (Lumpectomy: 5.6% vs Mastectomy: 1.8%; p = 0.43) (Table 4). There were no milk duct fistulas observed (Table 4). Seven of the PABC-PP patients (9.5%) required reoperation for surgical complications within 30 days of their initial surgery (Table 4). Indications for reoperation included flap necrosis (n = 3), removal of an infected tissue expander (n = 1), surgical site washout (n = 2), and recurrent chest wall mass (n = 1) in a patient with stage IV disease. Patients with PABC-PP were more likely to require reoperation than patients with PABC-P (PABC-P: 0% vs PABC-PP: 15.2%, n = 7; p = 0.04) (Table 4). There were two readmissions during this period of time (2.7%), both of whom were admitted after their reoperation (Table 4).

Postoperatively, 86.8% (n = 33) of patients received adjuvant endocrine therapy, 62.0% (n = 44) received adjuvant radiation, and 61.6% (n = 45) received adjuvant chemotherapy (Table 3). Patients diagnosed in the postpartum period were not significantly more likely to receive adjuvant radiation than patients diagnosed during pregnancy (PABC-P: 48.1%, n = 13 vs 70.5%, n = 31; p = 0.06) (Table 3). Likewise, patients who underwent lumpectomy were not

more likely to get radiation than patients who were treated with mastectomy (lumpectomy: 70.6%, n = 12 vs mastectomy: 59.3%, n = 32; p = 0.40). The median time in days to radiation after surgery, including patients treated with systemic therapy prior to radiation therapy, was not significantly different for PABC-P and PABC-PP (75.0 [IQR: 42.0, 191.0] vs 62.0 [IQR: 42.0, 156.0] days, p = 0.45).

Discussion

The incidence of surgical complications following breast surgery for women with PABC is unclear. Our study revealed low rates of complication in women undergoing lumpectomy (16.7%) or mastectomy (21.4%), demonstrating the feasibility and safety of breast conservation in this population. Notably, however, the majority (60%) of the total observed complications were seen in PABC-PP patients who had mastectomy with immediate reconstruction.

Pregnancy associated breast cancer (PABC) accounts for 0.2–2.8% of all breast cancers [8–12]. While PABC was originally felt to be “inoperable” based on the poor survival of patients with node positive disease, further research has shown that surgery is not only possible in women with PABC but also that there is also no difference in overall survival seen in patients managed with mastectomy versus lumpectomy for PABC [12–15]. In fact, prognosis is similar for women with PABC when compared to women with breast cancer matched for age, stage, race and tumor characteristics [9, 12, 14, 16, 17]. Surgical management for PABC, therefore, should be chosen by the same principles as non-PABC [3].

Surgical complications following conservative surgery for PABC are poorly studied. The largest publication detailing postoperative outcomes of patients with PACB reported a complication rate of 10% (n = 2) in the 20 patients treated with lumpectomy and 8.5% (n = 4) in the 47 patients undergoing mastectomy. These reported complications included one breast hematoma (10%) and one case of cellulitis (10%) in the patients undergoing lumpectomy and four cases of cellulitis (8.5%) in the patients treated with mastectomy [5]. Of note, this study defined postoperative complications to include cellulitis, abscess, hematoma or milk fistula, and did not specifically include other complications, like seroma, reported in our study [5]. Further, they did not specify the type of mastectomy performed or whether reconstruction was performed, both factors which could influence the observed postoperative complication rate [5]. In the present study, we report on 18 patients with PACB treated with lumpectomy, 16.7% (n = 3) of whom experienced a postoperative complication including seroma (16.7%, n = 3) and wound dehiscence (5.6%, n = 1) (Table 4). Seromas have been defined inconsistently in the literature, but are documented more frequently when symptomatic palpable, or requiring needle aspiration. In the current study, any seroma documented in the EMR was reported as a postoperative complication. This may ultimately result in an overestimate of the rate of seroma formation as well as the overall complication rate. Although it is difficult to compare the rate of complication directly to the study by Dominici et al, the observed complication rate in our patient population was within reported literature within the general population following lumpectomy for seroma (3–85%) and wound issues (0.5–15.9%) [5, 18–25].

Of the 56 patients treated with mastectomy, we observed a 27.2% (n = 12) postoperative complication rate (Table 4). Notably, 60% (n = 9) of these observed complications were seen in patients with PABC-PP who received mastectomy with immediate reconstruction. Reoperation for surgical complications within 30 days of the initial surgery was required in 9.5% (n = 7) of patients to address flap necrosis (n = 3), removal of an infected tissue expander (n = 1), surgical site washout (n = 2), and a recurrent chest wall mass (n = 1) in a patient with stage IV disease (Table 4). Two of these patients were readmitted postoperatively, accounting for the unplanned readmission rate of 2.7% within 30 days of surgery (Table 4). Overall, the rate of complications observed in our study population is comparable to

previously reported rates following mastectomy in both pregnant and non-pregnant cohorts [5–7, 26]. However, because the majority of complications in the current study were seen in patients who were treated with mastectomy with immediate reconstruction, careful counseling is warranted during the shared decision-making process, and consideration may be given to the option delayed reconstruction in patients deemed high risk.

Mammogenesis begins in utero, and the breast continues to develop during a woman's lifetime in response to hormonal cues [27]. During pregnancy and lactation, estrogen, progesterone, and prolactin induce a number of changes in the breast. Breast ducts and lobules increase in both number and size. Fibrofatty stroma involutes, and the fluid content of the breast increases. To aid in facilitating these changes, the vascularity of the breast also increases. These associated physiologic changes complicate imaging by increasing mammographic density and the increase in breast volume, firmness, and nodularity complicate physical exam [28–30]. It is possible that the physiologic changes in the breast during pregnancy and lactation could affect the frequency postoperative complications in patients with PABC, as seen in the present study. As such, it may be prudent to delay reconstruction in patients with PABC-PP treated with mastectomy and immediate reconstruction who are still lactating at the time of surgery. Another feared complication of breast biopsy and surgery in lactating women, the milk duct fistula, is defined as a fistulous tract between a lactiferous duct and the skin [31]. To date, however, there have been no reports of milk duct fistula in patients with PABC treated with lumpectomy, including our current study [5, 13].

While this study is limited by its retrospective nature and limited patient numbers, it represents the largest series of a well-characterized contemporary cohort of patients with PABC treated with breast surgery at a single institution. It is also the first to distinguish between the type of mastectomy performed and reconstruction. The sample size and relatively low incidence of postoperative outcomes were not powered for significance and did not allow for multivariable analysis given the rarity of PABC. Finally, our study focused on the immediate post-operative period, and therefore lacks long-term follow up, which may be more relevant to women undergoing mastectomy with reconstruction. Future research could benefit from the inclusion of additional patients with longer follow up and survival analysis.

In conclusion, in this single institution retrospective cohort study, there was no increased risk of postoperative complications in women with PABC on the basis of treatment with lumpectomy as compared to mastectomy or timing of diagnosis and treatment during pregnancy or postpartum. The most commonly observed complication after both lumpectomy and mastectomy was seroma formation. There is an increased risk of postoperative complications in patients with PABC-PP treated with mastectomy and immediate reconstruction, suggesting that delayed reconstruction may be beneficial in this population. Our findings can help to improve pre-operative counseling regarding post-operative expectations for complications in patients undergoing lumpectomy, mastectomy, and reconstruction.

Declarations

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Author Contributions – *All authors contributed to the study conception and design. Material preparation and data collection were performed by Anna Chichura, Ayat ElSherif, and Swapna Kollikonda. Data analysis was performed by Meng Yao, Anna Chichura, and Zahraa Al-Hilli. The first draft of the manuscript was written by Anna Chichura and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.*

Data Availability – *The datasets generated during and/or analysed during the current study are not publicly available but are available from the corresponding author on reasonable request.*

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Tables

Table 1. Patient Characteristics

Factor	Total (N=74)	PABC-P (N=28)	PABC-PP (N=46)	p-value
Age at Diagnosis	34.5 ± 3.8	34.4 ± 3.4	34.5 ± 4.0	0.87[a]
BMI	27.0 [22.5, 31.2]	27.8 [22.8, 31.6]	26.1 [22.5, 31.0]	0.52[b]
Medical Comorbidities				
Obesity	24 (32.4)	10 (35.7)	14 (30.4)	0.64[c]
GDMA1	1 (1.4)	1 (3.6)	0 (0.00)	0.38[d]
GDMA2	1 (1.4)	0 (0.00)	1 (2.2)	0.99[d]
Hypothyroidism	1 (1.4)	0 (0.00)	1 (2.2)	0.99[d]
Asthma	5 (6.8)	3 (10.7)	2 (4.3)	0.36[d]
Psychiatric illness^	11 (14.9)	2 (7.1)	9 (19.6)	0.19[d]
Tobacco use	9 (12.2)	4 (14.3)	5 (10.9)	0.72[d]
Other	11 (14.9)	2 (7.1)	9 (19.6)	0.19[d]
None	30 (40.5)	11 (39.3)	19 (41.3)	0.86[c]
Obstetric Outcomes				
GA at diagnosis (weeks)		27.1 [9.8, 32.6]		
GA at surgery (weeks)		34.2 [15.9, 52.6]		
GA at delivery (weeks)		37.4 [35.6, 39.0]		
Presentation				
Duration of symptoms prior to presentation (months)	1.00 [0.25, 4.0]	1.99 [0.25, 5.0]	1.00 [0.25, 3.0]	0.75[b]
Palpable mass (Patient)	64 (86.5)	26 (92.9)	38 (82.6)	0.30[d]
Palpable mass (Physician)	3 (4.1)	0 (0.00)	3 (6.5)	0.28[d]
Itching	1 (1.1)	0 (0.00)	1 (2.2)	0.99[d]
Pain	13 (17.6)	7 (25.0)	6 (13.0)	0.22[d]
Imaging	2 (2.7)	0 (0.00)	2 (4.3)	0.52[d]
Decreased milk production	3 (4.1)		3 (6.5)	
Change in bra size	2 (2.7)	0 (0.00)	2 (4.3)	0.52[d]
Benign biopsy	1 (1.4)	0 (0.00)	1 (2.2)	0.99[d]

Erythema	5 (6.8)	2 (7.1)	3 (6.5)	0.99[d]
Presumed abscess	2 (2.7)	0 (0.00)	2 (4.3)	0.52[d]
Axillary lymphadenopathy	1 (1.4)	0 (0.00)	1 (2.2)	0.99[d]
Nipple retraction	2 (2.7)	0 (0.00)	2 (4.3)	0.52[d]
Genetic Testing Performed*	67 (90.5)	23 (82.1)	44 (95.7)	0.097[d]
Genetic Mutation*	**(N=67)**	**(N=23)**	**(N=44)**	
Wildtype (none)	35 (52.2)	7 (30.4)	28 (63.6)	***0.01[c]***
BRCA 1	16 (23.9)	6 (26.1)	10 (22.7)	0.76[d]
BRCA 2	3 (4.5)	1 (4.3)	2 (4.5)	0.99[d]
VUS	11 (16.4)	7 (30.4)	4 (9.1)	**0.04[d]**
BARD1	1 (1.5)	1 (4.3)	0 (0.00)	0.34[d]

PABC-P, pregnancy associated breast cancer diagnosed during pregnancy; PABC-PP, pregnancy associated breast cancer diagnosed after pregnancy; BMI, body mass index; GDMA1, non-insulin dependent gestational diabetes mellitus (type 1); GDMA2, insulin dependent gestational diabetes mellitus type 2; GA, gestational age; BRCA 1, breast cancer type 1 susceptibility gene; BRCA 2, breast cancer type 2 susceptibility gene; VUS, variant of uncertain significance; BARD1, BRCA1-associated RING domain 1 gene

^Includes anxiety, depression

*Missing values

Categorical variables are presented as n (%); continuous variables are presented as mean with interquartile range [25, 75] or ± standard deviation; p-values: a=t-test, b=Wilcoxon Rank Sum test, c=Pearson's chi square test, d=Fisher's Exact test.

Table 2. Tumor Characteristics and Staging

	Total (N=74)	PABC-P (N=28)	PABC-PP (N=46)	p-value
Histology				
Surgical Pathology				
Infiltrating ductal	48 (64.9)	22 (78.6)	26 (56.5)	0.054[c]
Invasive lobular	3 (4.1)	1 (3.6)	2 (4.3)	0.99[d]
Mixed ductal and lobular	5 (6.8)	1 (3.6)	4 (8.7)	0.64[d]
Mucinous	1 (1.4)	0 (0.00)	1 (2.2)	0.99[d]
Spindle cell metaplastic carcinoma	2 (2.7)	1 (3.6)	1 (2.2)	0.99[d]
Fibroepithelial Lesion	1 (1.4)	0 (0.00)	1 (2.2)	0.99[d]
DCIS	30 (40.5)	11 (39.3)	19 (41.3)	0.86[c]
Malignant Phylloides	1 (1.4)	0 (0.00)	1 (2.2)	0.99[d]
Pathologic complete response^	13 (38.2)	3 (33.3)	10 (40.0)	0.99[d]
Histologic Grade*	*(N=72)*	*(N=28)*	*(N=44)*	0.62[d]
1	5 (6.9)	1 (3.6)	4 (9.1)	
2	18 (25.0)	6 (21.4)	12 (27.3)	
3	49 (68.1)	21 (75.0)	28 (63.6)	
Receptor Status				
ER-/PR-/HER2-	22 (29.7)	9 (32.1)	13 (28.3)	0.72[c]
ER+ or PR+	43 (58.1)	16 (57.1)	27 (58.7)	0.90[c]
HER2+	19 (25.7)	7 (25.0)	12 (26.1)	0.92[c]
Staging - Clinical*	*(N=72)*	*(N=27)*	*(N=45)*	0.18[d]
0	5 (6.9)	1 (3.7)	4 (8.9)	
IA	12 (16.7)	2 (7.4)	10 (22.2)	
IB	1 (1.4)	1 (3.7)	0 (0.00)	
IIA	24 (33.3)	12 (44.4)	12 (26.7)	
IIB	10 (13.9)	5 (18.5)	5 (11.1)	
IIIA	11 (15.3)	4 (14.8)	7 (15.6)	
IIIB	2 (2.8)	0 (0.00)	2 (4.4)	
IIIC	3 (4.2)	2 (7.4)	1 (2.2)	

IV	4 (5.6)	0 (0.00)	4 (8.9)

PABC-P, pregnancy associated breast cancer diagnosed during pregnancy; PABC-PP, pregnancy associated breast cancer diagnosed after pregnancy

^Presented as percentage of patients that received neoadjuvant chemotherapy

* missing values

Categorical variables are presented as n (%); p-values: c=Pearson's chi-square test, d= Fisher’s Exact test.

Table 3. Treatment

Factor	Total (N=74)	PABC-P (N=28)	PABC-PP (N=46)	p-value
Neoadjuvant treatment				
Chemotherapy	34 (45.9)	9 (32.1)	25 (54.3)	0.06[c]
Surgery				0.92[c]
Lumpectomy	18 (24.3)	7 (25.0)	11 (23.9)	
Mastectomy	56 (75.7)	21 (75.0)	35 (76.1)	
Simple mastectomy	9 (12.2)	6 (21.4)	3 (6.5)	0.07[d]
Skin sparing mastectomy	16 (21.6)	4 (14.3)	12 (26.1)	0.23[d]
Nipple sparing mastectomy	8 (10.8)	2 (7.1)	6 (13.0)	0.70[d]
Modified radical mastectomy	23 (31.1)	9 (32.1)	14 (30.4)	0.88[c]
Reconstruction*	**(N=56)**	**(N=21)**	**(N=35)**	
Immediate	32 (57.1)	9 (42.9)	23 (65.7)	0.094[c]
Type of immediate reconstruction				0.31[c]
Tissue expander	26 (46.4)	8 (38.1)	18 (51.4)	
Direct to implant	3 (5.4)	0 (0.00)	3 (8.6)	
Flap	3 (5.4)	1 (4.8)	2 (5.7)	
None	24 (42.9)	12 (57.1)	12 (34.3)	
Delayed	3 (5.4)	2 (9.5)	1 (2.9)	0.55[d]
Sentinel lymph node biopsy	35 (47.3)	11 (39.3)	24 (52.2)	0.28[c]
Axillary dissection	6 (8.1)	4 (14.3)	2 (4.3)	0.19[d]
Contralateral prophylactic surgery	32 (43.2)	11 (39.3)	21 (45.7)	0.59[c]
-				
Patents requiring margin re-excision	9 (12.2)	3 (10.7)	6 (13.0)	0.99[d]
-				
Adjuvant treatment				

Chemotherapy	45 (61.6)	21 (75.0)	24 (53.3)	0.64[c]
Endocrine therapy^	33 (86.8)	11 (78.6)	22 (91.7)	0.34[c]
Radiation^^	44 (62.0)	13 (48.1)	31 (70.5)	0.06[c]

PABC-P, pregnancy associated breast cancer diagnosed during pregnancy; PABC-PP, pregnancy associated breast cancer diagnosed after pregnancy

*Reported as percentage of patients who underwent mastectomy

^Reported as percentage of patients with hormone receptor positive disease, PABC-P (N=14), PABC-PP

(N=24)

^^ Missing values, PABC-P (N=27), PABC-PP (N=44)

Statistics presented as N (column %); p-values: c=Pearson's chi square test, d=Fisher's Exact test.

Table 4. Postoperative complications

		Timing of diagnosis			Surgery performed		
Factor	**Total (N=74)**	**PABC-P (N=28)**	**PABC-PP (N=46)**	**p-value**	**Lumpectomy (N=18)**	**Mastectomy (N=56)**	**p-value**
Complications*							
Any	15 (20.3)	3 (10.7)	12 (26.0)	0.11[d]	3 (16.7)	12 (21.4)	0.99[d]
Seroma	8 (10.8)	3 (10.7)	5 (10.9)	0.99[d]	3 (16.7)	5 (8.9)	0.39[d]
Partial nipple necrosis	1 (1.4)	0 (0.00)	1 (2.2)	0.99[d]	0 (0.00)	1 (1.8)	0.99[d]
Full nipple necrosis	0 (0.00)	0 (0.00)	0 (0.00)		0 (0.00)	0 (0.00)	
Partial/full thickness skin flap necrosis	3 (4.1)	0 (0.00)	3 (6.5)	0.28[d]	0 (0.00)	3 (5.4)	0.99[d]
Milk fistula	0 (0.00)	0 (0.00)	0 (0.00)		0 (0.00)	0 (0.00)	
Superficial surgical site infection	3 (4.1)	0 (0.00)	3 (6.5)	0.28[d]	0 (0.00)	3 (5.4)	0.99[d]
Deep surgical site infection	1 (1.4)	0 (0.00)	1 (2.2)	0.99[d]	0 (0.00)	1 (1.8)	0.99[d]
Wound dehiscence	2 (2.7)	1 (3.6)	1 (2.2)	0.99[d]	1 (5.6)	1 (1.8)	0.43[d]
Hematoma	0 (0.00)	0 (0.00)	0 (0.00)		0 (0.00)	0 (0.00)	
Within 30 days of surgery:							
Reoperation	7 (9.5)	0 (0.00)	7 (15.2)	**0.04[d]**	1 (5.6)	6 (10.7)	0.99[d]
Unplanned readmission	2 (2.7)	0 (0.00)	2 (4.3)	0.52[d]	0 (0.00)	2 (3.6)	0.99[d]

PABC-P, pregnancy associated breast cancer diagnosed during pregnancy; PABC-PP, pregnancy associated breast cancer diagnosed after pregnancy

*Not listed in table (Count=0): organ space surgical site infection, pneumonia, urinary tract infection, sepsis, septic shock, failure to wean, reintubation, intraoperative anesthetic complications, deep vein thrombosis, pulmonary embolism, acute renal failure, progressive renal insufficiency, peripheral nerve deficit, cerebral vascular accident, coma, myocardial infection, cardiac arrest, transfusion, death

Statistics presented as N (column %); p-values: d=Fisher's Exact test.