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Article

Breastfeeding after breast cancer in young *BRCA* carriers

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Abstract

Background: We investigated safety of breastfeeding after breast cancer in patients carrying germline *BRCA* pathogenic or likely pathogenic variants.

Methods: This was an international, multicenter, hospital-based, retrospective cohort study including *BRCA* carriers diagnosed with stage I–III invasive breast cancer at age 40 years or younger between January 2000 and December 2020 (NCT03673306). Locoregional recurrences and/or contralateral breast cancers, disease-free survival (DFS), and overall survival (OS) were compared between patients who breastfed after delivery and those who did not.

Results: Among 4732 patients included from 78 centers worldwide, 659 had a pregnancy after breast cancer diagnosis, of whom 474 delivered a child. After excluding patients with uptake of bilateral risk-reducing mastectomy prior to delivery ($n = 225$) or unknown breastfeeding status ($n = 71$), 110 (61.8%) breastfed (median duration 5 months) and 68 (38.2%) did not breastfeed. Compared to patients in the no breastfeeding group, those who breastfed were more frequently nulliparous at breast cancer diagnosis (61.8% vs 45.6%) and did not report prior smoking habit (71.8% vs 57.4%). After a median follow-up of 7.0 years following delivery, 7-year cumulative incidence of locoregional recurrences and/or contralateral breast cancers was 29% in the breastfeeding group and 36% in the no breastfeeding group (adjusted subdistribution hazard ratio [HR] = 1.08, 95% CI = 0.57 to 2.06). No difference in DFS (adjusted hazard ratio [aHR] = 0.83, 95% CI = 0.49 to 1.41) nor in OS (aHR = 1.32, 95% CI = 0.31 to 5.66) was observed.

Conclusions: Breastfeeding did not appear to be associated with a higher risk of developing locoregional recurrences or contralateral breast cancers, emphasizing the possibility of achieving a balance between maternal and infant needs without compromising oncological safety.

Introduction

Breast cancer is the most common malignancy affecting young women during their reproductive years.[1] Germline *BRCA* genetic testing is recommended for all young patients, regardless of family history or tumor biology,[2] given more than 12% of young patients with breast cancer are expected to carry a germline pathogenic or likely pathogenic variant (PV) in the *BRCA1* and/or *BRCA2* genes.[3] In this patient population, additional reproductive considerations apply.[4] Several studies demonstrated that pregnancy after diagnosis and treatment for breast cancer is safe with no associated increased risk of breast cancer recurrence,[5] including among *BRCA* carriers.[6]

For women with prior history of breast cancer who become pregnant and have a live birth, breastfeeding can be a complex and emotional decision. Breast cancer treatment, especially surgery and radiotherapy, can impact a woman's ability to breastfeed.[7,8] Approximately 80% of patients undergoing breast conserving surgery combined with radiotherapy experience reduced breast enlargement during pregnancy, with around 50% of them experiencing limited postnatal milk production from the ipsilateral breast.[9-11]

In the general population, several studies suggested a protective effect of breastfeeding on the risk of developing breast cancer,[12] including the most aggressive form of triple-negative disease.[13] A similar protective effect of breastfeeding on the risk of breast cancer development was observed for *BRCA1* carriers but not for *BRCA2* carriers.[14] Very limited evidence is available regarding the potential benefits or risks of breastfeeding in young breast cancer survivors.[15,16] For survivors who carry a *BRCA1* or *BRCA2* PV, the decision to breastfeed after breast cancer is even more complex considering their higher risk of new primary breast cancer in the remaining breast tissue and the indication for consideration of risk-reducing mastectomy.[17]

The BRCA BCY collaboration (NCT03673306) is the largest network of *BRCA* carriers with a history of breast cancer diagnosed at the age of 40 years or younger. Out of 4732 included patients, 659 had at least 1 pregnancy after breast cancer,[6] representing a unique opportunity to evaluate the safety of breastfeeding in this special population.

Methods

Study design, setting, and patients

This was an international, multicenter, hospital-based, retrospective cohort study including young *BRCA* carriers with a history of breast cancer. As previously reported,[6] eligible patients were women diagnosed at the age of 40 years or younger with invasive breast cancer between January 2000 and December 2020 and known to carry a germline PV in the *BRCA1* and/or *BRCA2* genes. For this analysis, only patients with a live birth after breast cancer were included.

Data collection and study oversight

Collected data included breast cancer history and treatment, *BRCA* PV, risk-reducing surgeries, reproductive outcomes, recurrences and survival. Diagnostic, treatment, and follow-up procedures were conducted according to the clinical practice of each center. Pregnancy status, its outcomes and breastfeeding were determined using medical records or through patient self-reports collected during follow-up visits or surveys, depending on the center.

The Institut Jules Bordet (Brussels, Belgium) was the coordinating center and served as the central ethics committee. The study received ethics approval by the local, regional, or national institutional review boards of participating centers whenever required by local regulatory authorities. Written informed

consent was obtained from participants before inclusion in centers with this requirement.

Reporting of the present work followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[18]

Study objectives

The primary objective of the present analysis was to evaluate the association between breastfeeding and the development of locoregional recurrences and/or contralateral breast cancers. Secondary objectives were to evaluate the association between pregnancy, fetal, and obstetric outcomes and breastfeeding status as well as the association between breastfeeding and survival outcomes.

The primary endpoint was locoregional recurrences and/or contralateral breast cancers. Secondary endpoints included pregnancy, fetal, and obstetric outcomes, disease-free survival (DFS) and overall survival (OS). Disease-free survival and OS were computed according to Standardized Definitions for Efficacy End Points (STEEP) criteria.[19]

Young *BRCA* carriers with a live birth after breast cancer were divided into 4 groups: women who breastfed (breastfeeding group), women who did not breastfeed (no breastfeeding group), women who underwent risk-reducing mastectomy before delivery (not able to breastfeed), and women with unknown breastfeeding status.

Women who underwent bilateral risk-reducing mastectomy before delivery and women with unknown breastfeeding status were included only in descriptive analysis. To evaluate the safety of breastfeeding, only patients in the breastfeeding and no breastfeeding groups were included.

Statistical analysis

Cumulative incidence of locoregional recurrences and/or contralateral breast cancers was estimated using a competing risk model. Distant recurrences, second primary malignancies, and death without recurrence were considered competing events. The Fine and Gray model was used to estimate the corresponding subdistribution hazard ratio (sHR) and to adjust for covariates.[20] Adjustment was made for patient or tumor characteristics unbalanced between the groups as well as for known prognostic factors. Final adjustment was made for country, smoking habit, tumor grading, nodal status, hormone receptor status, and uptake of risk-reducing surgeries. Risk-reducing mastectomy after delivery and risk-reducing salpingo-oophorectomy were included in the model as time-dependent covariates.

The Kaplan–Meier method was used to estimate DFS and OS. Unadjusted and adjusted Cox models were used to compare DFS and OS according to breastfeeding status. All survival endpoints were computed from the date of delivery. Patients without the events of interest were censored at the time of last follow-up.

Subgroup analyses were performed according to specific *BRCA* gene, time from breast cancer diagnosis to conception (ie, pregnancy interval), hormone receptor status, and use of prior chemotherapy.

The following parameters about pregnancy, fetal, and obstetric outcomes were compared between patients in the breastfeeding and no breastfeeding groups: patient age at delivery, time from breast cancer diagnosis to delivery (ie, pregnancy interval), type of conception, number of live births at the first pregnancy after breast cancer, number of preterm (<37 weeks) or full-term (≥37 weeks) pregnancies, congenital malformations, pregnancy, and/or obstetric complications.

All statistical analyses were 2-sided with $P < .05$ considered statistically significant. No adjustment for multiple comparison was made. Analyses were performed using SAS version 9.4 (SAS Institute Inc.).

Results

Among the 4732 patients eligible for the study from 78 centers worldwide, 659 had a pregnancy after breast cancer diagnosis. After excluding patients with ongoing pregnancy, women that experienced abortions or miscarriages and those with a DFS event before delivery, 474 patients delivered a child (Figure 1).

Among the included patients, 110 breastfed their child, 68 did not breastfeed, 225 underwent bilateral risk-reducing mastectomy before delivery (thus were not able to breastfeed), and 71 had unknown breastfeeding status. Patient and tumor characteristics in the 4 groups are reported in Table S1.

After exclusion of patients with uptake of bilateral risk-reducing mastectomy and patients with unknown breastfeeding status, 178 patients were included in the primary analysis, of whom 110 (61.8%) breastfed and 68 (38.2%) did not breastfeed. Compared to patients in the no breastfeeding group, those in the breastfeeding group were more frequently nulliparous at the time of breast cancer diagnosis (61.8% vs 45.6%, $P = .026$) and did not report prior smoking habit (71.8% vs 57.4%, $P = .019$) (Table 1). Overall, 114 (64.0%) patients had undergone breast conserving surgery with radiotherapy and 164 (92.1%) had received (neo) adjuvant chemotherapy (Table 1). Among patients that breastfed, median duration of breastfeeding was 5 months ([IQR] 2-6 months).

Compared to patients in the no breastfeeding group, those in the breastfeeding group more frequently had a singleton pregnancy (90.9% vs 79.4%, $P = .029$; Table 2). Otherwise, no difference in pregnancy, fetal, or obstetrical outcomes was observed between the two groups. Among patients that breastfed, median age at delivery was 35.4 years (IQR 31.7-37.7 years) and median time from breast cancer diagnosis to delivery was 4.1 years (IQR 2.9-6.0 years). The majority of pregnancies occurred through spontaneous conception (80.0%) and were at term (80.0%) with no complications (73.6%).

Patient and tumor characteristics between patients in the breastfeeding and no breastfeeding groups according to specific *BRCA* gene are reported in Table S2.

After a median follow-up of 7.0 years (IQR 3.6-10.5 years) following delivery, 55 (30.9%) patients experienced locoregional recurrences or a contralateral breast cancer and 16 (9.0%) experienced a competing event (Table S3). No difference in cumulative incidence of locoregional recurrences and/or contralateral breast cancer events between the breastfeeding and no breastfeeding groups was observed (Figure 2). The 7-year cumulative incidence of locoregional recurrences and/or contralateral breast cancers was 29% (95% CI = 20 to 40) in the breastfeeding group and 36% (95% CI = 23 to 49) in the no breastfeeding group (unadjusted sHR = 0.84, 95% CI = 0.49 to 1.44, $P = .531$; adjusted sHR = 1.08, 95% CI = 0.57 to 2.06, $P = .518$).

Results of the subgroups analyses are reported in Table 3. No statistically significant interaction in the analysis of cumulative incidence of locoregional recurrences and/or contralateral breast cancer events was observed between the explored subgroups (specific *BRCA* gene, pregnancy interval, hormone receptor status, and chemotherapy use) and breastfeeding status.

Overall, 71 DFS events were observed, 42 (38.2%) in patients that breastfed and 29 (42.7%) in patients that did not breastfeed

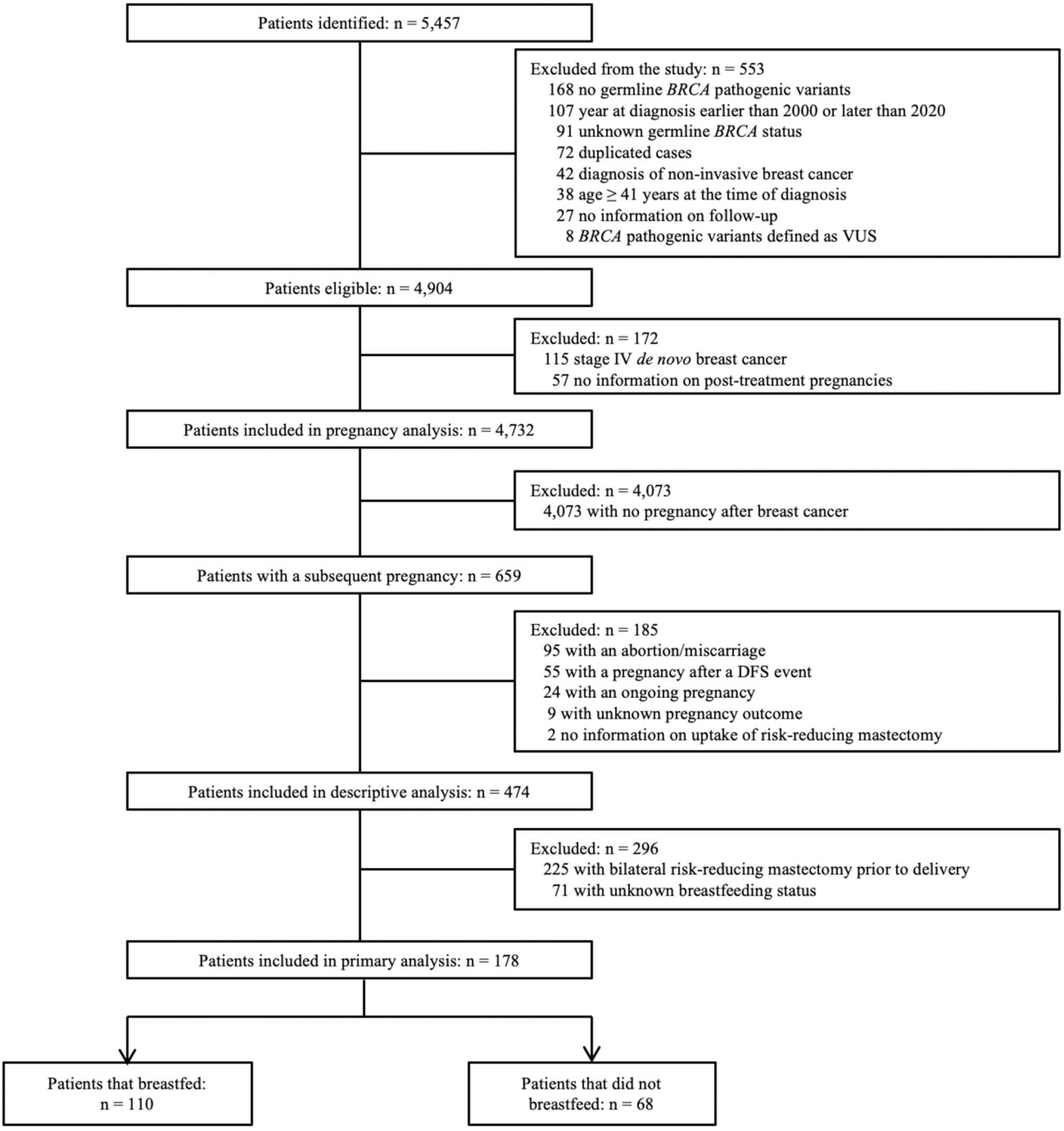


Figure 1. Study flow chart. Abbreviation: VUS = variant of unknown significance.

(Table S3). Seven-year DFS was 62% (95% CI = 50 to 71) and 54% (95% CI = 40 to 66) in patients that breastfed and that did not breastfeed, respectively (unadjusted HR = 0.79, 95% CI = 0.49 to 1.27, $P = .333$; adjusted HR [aHR] = 0.83, 95% CI = 0.49 to 1.41, $P = .096$) (Figure 3, A). The pattern of first DFS event in the breastfeeding and no breastfeeding groups according to specific *BRCA* gene is reported in Table S4.

Overall, 12 OS events were observed, 9 (8.2%) in patients that breastfed and 3 (4.4%) in patients that did not breastfeed. Seven-year OS was 92% (95% CI = 84 to 97) and 93% (95% CI = 79 to 98) in patients that breastfed and that did not breastfeed, respectively (unadjusted HR = 1.78, 95% CI = 0.48 to 6.59, $P = .365$; aHR = 1.32, 95% CI = 0.31 to 5.66, $P = .117$) (Figure 3, B).

Discussion

In this large global study of young *BRCA* carriers with a subsequent live birth after prior breast cancer, nearly two thirds (61.8%) of patients breastfed after delivery. Patients who breastfed were more frequently nulliparous at the time of breast

Table 1. Patient and tumor characteristics at breast cancer diagnosis between patients who breastfed after delivery and those who did not.

	Breastfeeding group $n = 110$ (%)	No breastfeeding group $n = 68$ (%)	*P*
Region			.027
Latin/South America	3 (2.7)	0 (0.0)	
Australia/Oceania	7 (6.4)	1 (1.5)	
Northern Europe	15 (13.6)	5 (7.4)	
Eastern Europe	6 (5.5)	0 (0.0)	
North America	6 (5.5)	1 (1.5)	
Southern Europe	51 (46.4)	45 (66.2)	
Asia	22 (20.0)	16 (23.5)	
Children before diagnosis			.026
No	68 (61.8)	31 (45.6)	
Yes	33 (30.0)	34 (50.0)	
Unknown	9 (8.2)	3 (4.4)	
Smoking habit			.019
Never smoker	79 (71.8)	39 (57.4)	
Ever smoker	16 (14.6)	22 (32.4)	
Unknown	15 (13.6)	7 (10.3)	
Year at diagnosis			.477
2000-2004	24 (21.8)	14 (20.6)	
2005-2008	26 (23.6)	19 (27.9)	
2009-2012	35 (31.8)	14 (20.6)	
2013-2016	18 (16.4)	14 (20.6)	
2017-2020	7 (6.4)	7 (10.3)	
Age at diagnosis, median (IQR) years	30 (28-33)	30 (29-32)	.882
Age at diagnosis			.506
≤30 years	58 (52.7)	38 (55.9)	
31-35 years	42 (38.2)	27 (39.7)	
36-40 years	10 (9.1)	3 (4.4)	
Specific *BRCA* gene			
BRCA1	80 (72.7)	53 (77.9)	.653
BRCA2	29 (26.4)	14 (20.6)	
BRCA1 & *BRCA2*	1 (0.9)	1 (1.5)	
BRCA mutated, unknown if *BRCA1* or *BRCA2*	0 (0.0)	0 (0.0)	
Tumor grade			.964
G1	1 (0.9)	1 (1.5)	
G2	17 (15.5)	11 (16.2)	
G3	75 (68.2)	47 (69.1)	
Unknown	17 (15.5)	9 (13.2)	
Tumor size			.185
T1 (≤2 cm)	53 (48.2)	25 (36.8)	
T2 (>2 to ≤5 cm)	43 (39.1)	31 (45.6)	
T3 (>5 cm) or T4	11 (10.0)	6 (8.8)	
Missing	3 (2.7)	6 (8.8)	
Nodal status			.448
N0	68 (61.8)	40 (58.8)	
N1	34 (30.9)	18 (26.5)	
N2 or N3	5 (4.6)	6 (8.8)	
Unknown	3 (2.7)	4 (5.9)	
Hormone receptor status			.595
ER and PR negative	72 (65.5)	43 (63.2)	
ER and/or PR positive	36 (32.7)	22 (32.4)	
Unknown	2 (1.8)	3 (4.4)	
HER2 status			.282
HER2 negative	98 (89.1)	63 (92.6)	
HER2 positive	4 (3.6)	0 (0.0)	
Unknown	8 (7.3)	5 (7.4)	
Locoregional treatment			.816
Breast conserving surgery with radiotherapy	73 (66.4)	41 (60.3)	
Breast conserving surgery without radiotherapy	2 (1.8)	2 (2.9)	
Radical surgery with radiotherapy	17 (15.5)	11 (16.2)	
Radical surgery without radiotherapy	15 (13.6)	12 (17.7)	
Unknown	3 (2.7)	2 (2.9)	
Use of chemotherapy			.709
No	8 (7.3)	6 (8.8)	
Yes	102 (92.7)	62 (91.2)	
Use of endocrine therapy[a]			.806
No	4 (11.1)	2 (9.1)	
Yes	32 (88.9)	20 (90.9)	

Abbreviations: ER = estrogen receptor; G = tumor grade; IQR = interquartile range; N = nodal status; PR = progesterone receptor; T = tumor size.
[a] Calculated among patients with hormone receptor-positive breast cancer.

Table 2. Pregnancy, fetal, and obstetric outcomes between patients who breastfed after delivery and those who did not.

	Breastfeeding group, *n* = 110 (%)	No breastfeeding group, *n* = 68 (%)	*P*
Age at the time of delivery, median (IQR) years	35.4 (31.7-37.7)	35.1 (32.6-36.7)	.527
Time from breast cancer diagnosis to delivery, median (IQR) years	4.1 (2.9-6.0)	3.8 (3.0-5.9)	.682
Pregnancy interval			.672
≤5 years from diagnosis	71 (64.5)	46 (67.6)	
>5 years from diagnosis	39 (35.5)	22 (32.4)	
Type of conception			.794
Spontaneous pregnancy	88 (80.0)	52 (76.5)	
Use of assisted reproductive technology	11 (10.0)	9 (13.2)	
Unknown	11 (10.0)	7 (10.3)	
Number of live births at the first pregnancy after breast cancer			.029
1	100 (90.9)	54 (79.4)	
≥2	10 (9.1)	14 (20.6)	
Timing of delivery			.608
At term (≥37 weeks)	88 (80.0)	56 (82.4)	
Preterm (<37 weeks)	11 (10.0)	8 (11.8)	
Unknown	11 (10.0)	4 (5.9)	
Pregnancy complications			.619
None	81 (73.6)	53 (77.9)	
Delivery complications	6 (5.5)	1 (1.5)	
Pregnancy complications	7 (6.4)	6 (8.8)	
Congenital abnormalities	0 (0.0)	0 (0.0)	
Fetal complications	1 (0.9)	1 (1.5)	
Other complications	0 (0.0)	0 (0.0)	
Missing	15 (13.6)	7 (10.3)	

Abbreviation: IQR = interquartile range.

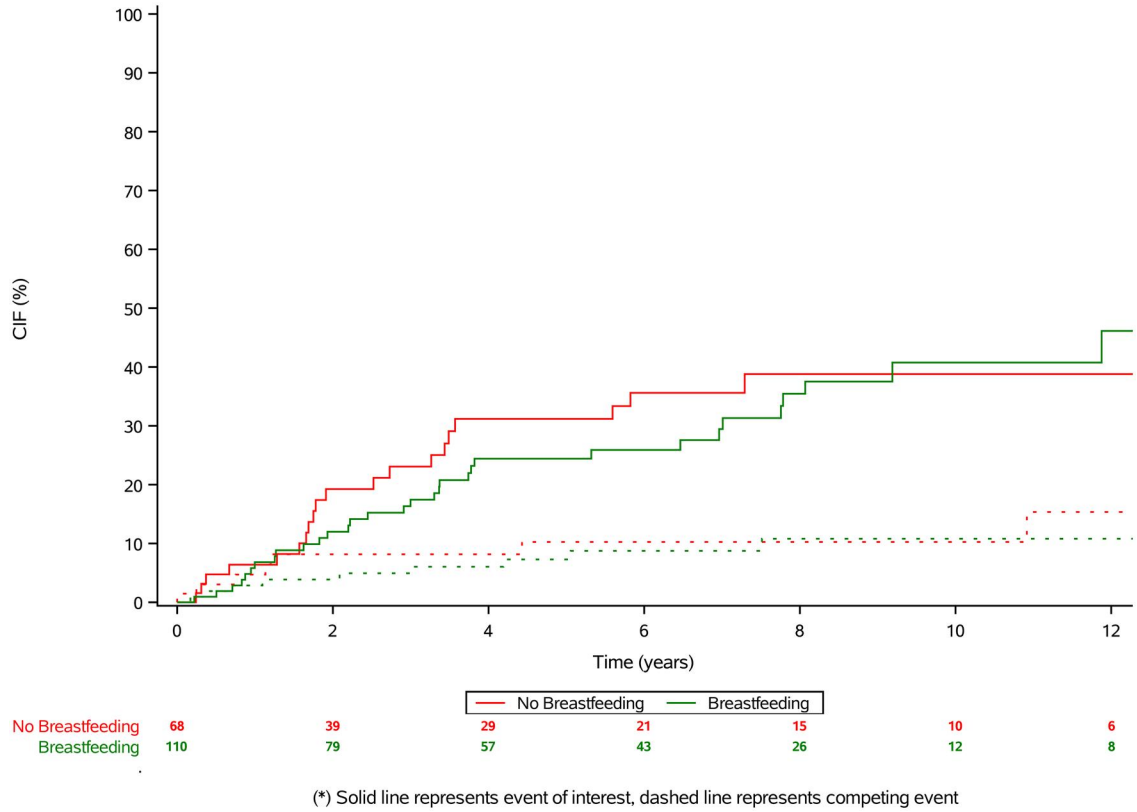


Figure 2. Cumulative incidence of locoregional recurrences and/or contralateral breast cancers between patients who breastfed after delivery and those who did not. CIF = cumulative incidence function.

Table 3. Subgroup analyses of cumulative incidence of locoregional recurrences and contralateral breast cancers.

Variable	Patients/Events/ Competing events	Univariate sHR (95% CI)	P[a]	Multivariate sHR (95% CI)	P[a]
Specific *BRCA* gene			.998		.840
BRCA1	133/38/9	0.88 (0.46 to 1.68)		1.20 (0.56 to 2.59)	
BRCA2	43/16/7	0.88 (0.34 to 2.52)		1.03 (0.29 to 3.67)	
Pregnancy interval			.141		.116
≤5 years	117/35/11	0.62 (0.33 to 1.19)		0.73 (0.35 to 1.55)	
>5 years	61/20/5	1.52 (0.56 to 4.11)		2.15 (0.68 to 6.79)	
Hormone receptor status			.728		.768
ER and PR negative	115/35/12	0.76 (0.39 to 1.49)		0.98 (0.45 to 2.14)	
ER and/or PR positive	58/19/4	0.93 (0.38 to 2.25)		1.22 (0.37 to 4.00)	
Use of chemotherapy			.184		.284
No	14/5/1	1.88 (0.58 to 6.11)		2.23 (0.56 to 8.89)	
Yes	164/50/15	0.78 (0.44 to 1.39)		0.97 (0.49 to 1.93)	

Abbreviations: CI = confidence intervals; ER = estrogen receptor; PR = progesterone receptor; sHR = hazard ratio.
[a] *P*-value for interaction.

cancer diagnosis, did not report prior smoking habit and had a singleton pregnancy. Breastfeeding did not appear to be associated with a higher risk of locoregional recurrences and/or contralateral breast cancers. These are the first results detailing the frequency and safety of breastfeeding in young breast cancer survivors who harbor germline *BRCA* PVs, and provide valuable insights for counseling this special patient population.

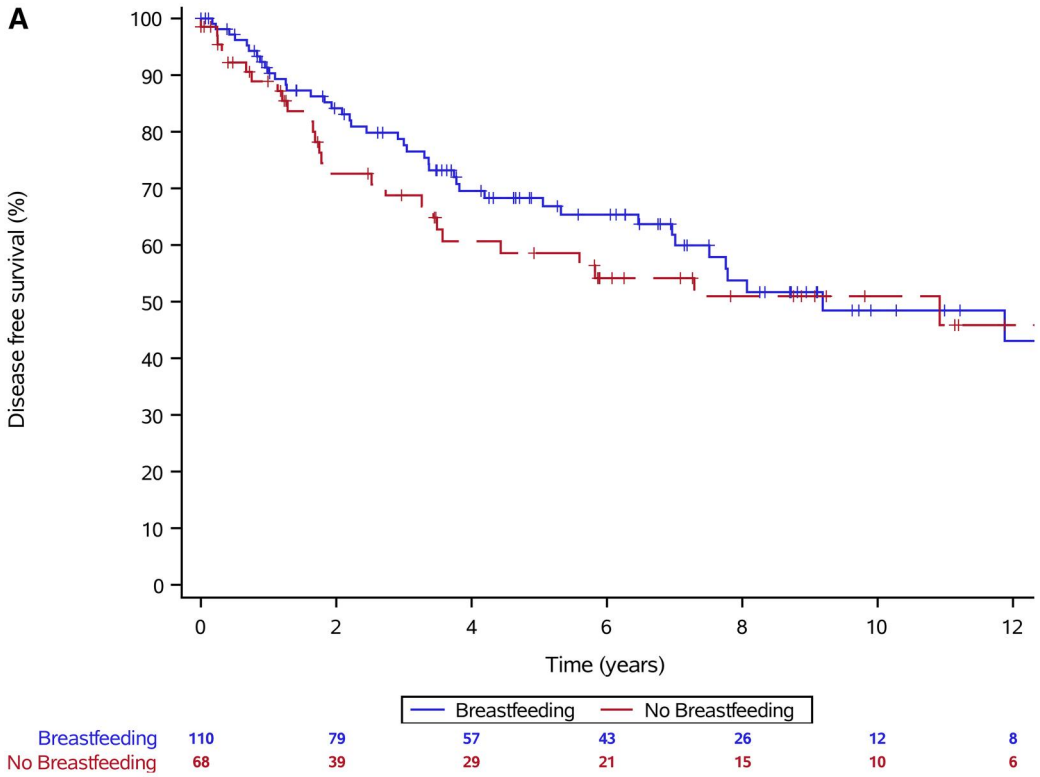
While limited available evidence suggests that breastfeeding after breast cancer is feasible,[11,15,21] to our knowledge, no prior study has tried to identify factors associated with breastfeeding, especially in *BRCA* carriers. In our study, as compared to patients that did not breastfeed, nulliparous women were more likely to breastfeed, suggesting that first-time mothers might be more motivated to breastfeed. Additionally, women who breastfed were more likely never smokers, indicating that lifestyle factors may be associated with the decision to breastfeed after breast cancer treatment.

Regarding maternal safety, prior evidence suggested that breastfeeding after breast cancer treatment did not appear to impact oncological outcomes; however, the sample size of these studies was very limited and no information on *BRCA* status was provided.[15,16] In our study, breastfeeding in *BRCA* carriers was not associated with a higher risk of locoregional recurrences and/or contralateral breast cancers. In *BRCA* carriers, young age at diagnosis of breast cancer is known to be associated with an increased risk of developing second primary breast cancers.[22,23] In our cohort, which included *BRCA* carriers with breast cancer diagnosis at a young age, 7-year cumulative incidence of locoregional recurrences and/or contralateral breast cancers was relatively high, being 29% in the breastfeeding group and 37% in the no breastfeeding group, with the majority of these events being second primary breast cancers (43 out of 55). Notably, for *BRCA* carriers, the increased risk of contralateral breast cancer and the beneficial effect of risk-reducing mastectomy in this special clinical setting should be considered during counseling and may play a crucial role in deciding to delay this surgical intervention in order to breastfeed.[24] With no increase in locoregional recurrences or contralateral breast cancers observed in either *BRCA1* or *BRCA2* carriers who breastfed, considering that pregnancies occurred a few years after breast cancer diagnosis, these results are encouraging, although further studies are needed to confirm these data.

Despite the known limited postnatal milk production from the irradiated breast,[15] patients and physicians should be informed that milk produced by the untreated breast may be sufficient for the nutritional needs of the newborn.[25] Guidelines recommend that women with prior history of breast cancer should be encouraged to breastfeed their children and that they should receive proper counseling in order to support unilateral breastfeeding, since misinformation is a major cause for avoiding breastfeeding.[26] However, no recommendation exists specifically for *BRCA* carriers with a history of breast cancer. Given that breastfeeding provides important nutritional and developmental benefits for infants,[27] our findings are helpful for informing these patients about their breastfeeding options.

In the interpretation of our results, some limitations should be acknowledged. This was a retrospective observational study. Information on breastfeeding was collected from oncological records and no information on breast side used for breastfeeding or the amount of milk production from the treated breast were collected. Furthermore, imbalances in patient and tumor characteristics between patients who breastfed after delivery and those who did not might have influenced long-term outcome results; however, survival models were adjusted for patient and tumor characteristics unbalanced between the groups as well as for known prognostic factors. Moreover, despite specific data quality control and data queries on this variable, 15% of the patients had missing information on breastfeeding uptake. Finally, given the frequency of bilateral mastectomy in this population, sample size was small precluding definitive conclusions. Despite these limitations, this is a unique cohort of young *BRCA* carriers, a relatively rare patient population, and it evaluated for the first time the safety of breastfeeding after breast cancer in this setting.

In conclusion, the decision to breastfeed after breast cancer among young *BRCA* carriers appears to be influenced by various factors, including parity and lifestyle factors. Nearly two thirds of patients who had a live birth after breast cancer opted to breastfeed without an apparent increase in the risk of developing locoregional recurrences or contralateral breast cancers. Our results provide novel information to guide health-care providers in the counseling of young *BRCA* carriers with breast cancer



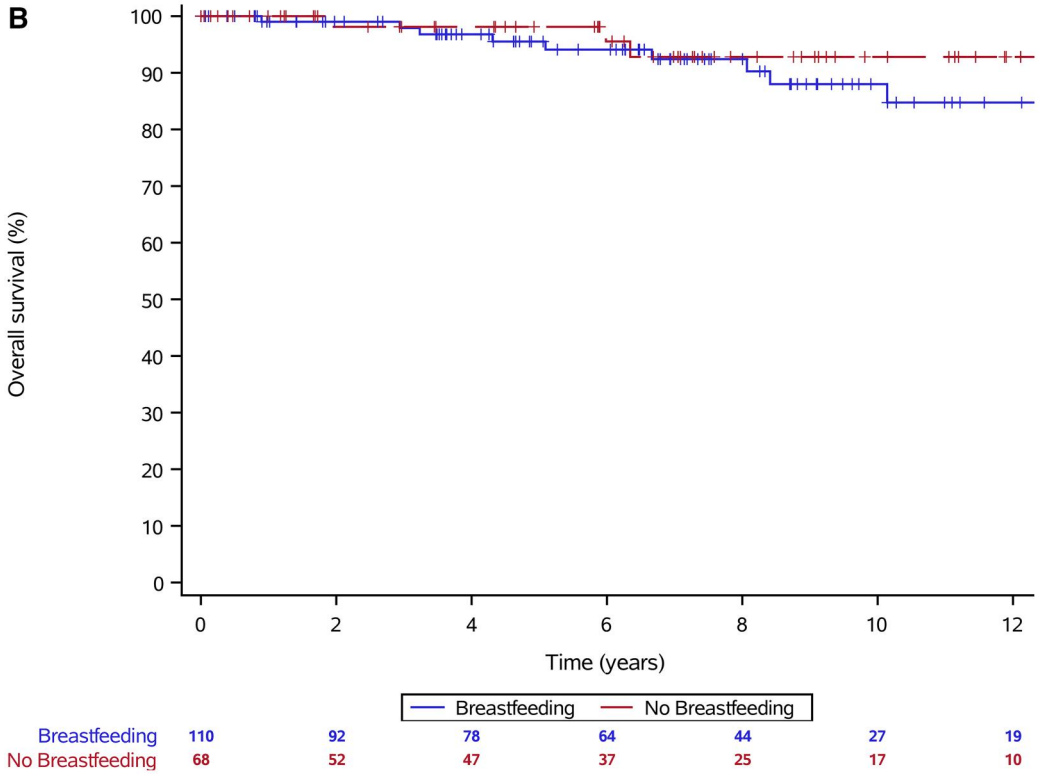


Figure 3. Survival outcomes between patients who breastfed after delivery and those who did not: (A) disease-free survival and (B) overall survival.

history who desire to breastfeed, emphasizing the possibility to achieve a balance between maternal and infant needs without compromising oncological safety. Further research is warranted to enhance our understanding of patients' needs and the implications of breastfeeding after breast cancer overall and particularly among *BRCA* carriers in order to further optimize their survivorship care.

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Author contributions

Eva Blondeaux (Conceptualization, Data curation, Formal analysis, Writing—original draft), Virginia Delucchi (Formal analysis, Writing—review & editing), Elene Mariamidze (Formal analysis, Writing—review & editing), Rinat Bernstein-Molho (Formal analysis, Writing—review & editing), Sophie Frank (Formal analysis, Writing—review & editing), Alberta Ferrari (Formal analysis, Writing—review & editing), Sabine Linn (Formal analysis, Writing—review & editing), Hee Jeong Kim (Formal analysis, Writing—review & editing), Elisa Agostinetto (Formal analysis, Project administration, Writing—review & editing), Shani Paluch-Shimon (Formal analysis, Writing—review & editing), Laura Cortesi (Formal analysis, Writing—review & editing), Antonio Di Meglio (Formal analysis, Writing—review & editing), Judith Balmana (Formal analysis, Writing—review & editing), Rinat Yerushalmi (Formal analysis, Writing—review & editing), Kenny A. Rodriguez-Wallberg (Formal analysis, Writing—review & editing), Tiphaine Renaud (Formal analysis, Writing—review & editing), Wanda Cui (Formal analysis, Writing—review & editing), Halle C.F. Moore (Formal analysis, Writing—review & editing), Stephanie M. Wong (Formal analysis, Writing—review & editing), Katarzyna Pogoda (Formal analysis, Writing—review & editing), Maryam Lustberg (Formal analysis, Writing—review & editing), Kelly-Anne Phillips (Formal analysis, Writing—review & editing), Sileny Han (Formal analysis, Writing—review & editing), Fabio Puglisi (Formal analysis, Writing—review & editing), Claudio Vernieri (Formal analysis, Writing—review & editing), Jyoti Bajpai (Formal analysis, Writing—review & editing), Amir Sonnenblick (Formal analysis, Writing—review & editing), Christine Rousset-Jablonski (Formal analysis, Writing—review & editing), Laura De Marchis (Formal analysis, Writing—review & editing), Ugo De Giorgi (Formal analysis, Writing—review & editing), Giampaolo Bianchini (Formal analysis, Writing—review & editing), Luis Texeira (Formal analysis, Writing—review & editing), Francois P. Duhoux (Formal analysis, Writing—review & editing), Cynthia Villarreal-Garza (Formal analysis, Writing—review & editing), Valentina Sini (Formal analysis, Writing—review & editing), Robert Fruscio (Formal analysis, Writing—review & editing), Lucia Del Mastro (Formal analysis, Writing—review & editing), Isabelle Demeestere (Formal analysis, Writing—review & editing), Hatem A. Azim (Formal analysis, Supervision, Writing—review & editing), Fedro A. Peccatori (Formal analysis, Supervision, Writing—review & editing), Ann H. Partridge (Formal analysis, Supervision, Writing—review & editing), and Matteo Lambertini (Conceptualization, Data curation, Formal analysis, Funding acquisition, Writing—original draft).

Supplementary material

Supplementary material is available at *JNCI: Journal of the National Cancer Institute* online.

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Conflicts of interest

E.B. reports speaker's fee from Eli Lilly, research funding (to the institution) from Gilead, all outside the submitted work. R.B.-M. reports honoraria for lectures from AstraZeneca, Roche, Pfizer; support for attending meetings from Pfizer (to the institution), AstraZeneca (to the institution), Gilead (to the institution), all outside the submitted work. E.A. reports speaker honoraria from Eli Lilly, AstraZeneca, Abscint, Bayer; advisory role for AstraZeneca; research grant to institution from Gilead; meeting/travel grants from Eli Lilly, AstraZeneca, Daiichi Sankyo, Abscint, Menarini, all outside the submitted work. A.D.M. reports speaker honoraria from Kephren and Techspert, all outside the submitted work. J.B. reports speaker honoraria and research at institution, AstraZeneca, all outside the submitted work. S.M.W. reports advisory role for Merck, AstraZeneca, all outside the submitted work. K.P. reports consultations/lectures/training/clinical trials and payment of conference fees from AstraZeneca, Gilead, Roche, Novartis, Eli Lilly, Pfizer, MSD, Swixx, all outside the submitted work. K.A.P. reports research funding to institution from AstraZeneca, all outside the submitted work. F.P. reports honoraria for advisory boards, activities as a speaker, travel grants from AstraZeneca, Daiichi Sankyo, Eisai, Eli Lilly, Exact Sciences, Gilead, Italfarmaco, Menarini, MSD, Novartis, Pfizer, Roche, and Seagen; research funding from AstraZeneca, Eisai, and Roche, all outside the submitted work. C.V. reports advisory role for Eli Lilly, Novartis, Pfizer, Menarini Stemline, Daiichi Sankyo; speaker honoraria from Eli Lilly, Menarini Stemline, MSD, Novartis,

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Data availability

Data will be available upon reasonable request to the corresponding author, after proper review of the data transfer agreement of each participating center and if ultimately allowed by local Ethics Committees.

References

1. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. *CA: Cancer J Clin*. 2023;73:17-48. https://doi.org/10.3322/caac.21763
2. Bedrosian I, Somerfield MR, Achatz MI, et al. Germline testing in patients with breast cancer: ASCO-Society of Surgical Oncology Guideline. *J Clin Oncol*. 2024;42:584-604. https://doi.org/10.1200/JCO.23.02225
3. Copson ER, Maishman TC, Tapper WJ, et al. Germline BRCA mutation and outcome in young-onset breast cancer (POSH): a prospective cohort study. *Lancet Oncol*. 2018;19:169-180. https://doi.org/10.1016/S1470-2045(17)30891-4
4. Buonomo B, Massarotti C, Dellino M, et al. Reproductive issues in carriers of germline pathogenic variants in the BRCA1/2 genes: an expert meeting. *BMC Med*. 2021;19:205. https://doi.org/10.1186/s12916-021-02081-7
5. Lambertini M, Blondeaux E, Bruzzone M, et al. Pregnancy after breast cancer: a systematic review and meta-analysis. *J Clin Oncol*. 2021;39:3293-3305. https://doi.org/10.1200/JCO.21.00535
6. Lambertini M, Blondeaux E, Agostinetto E, et al.; BRCA BCY Collaboration. Pregnancy after breast cancer in young BRCA carriers: an international hospital-based cohort study. *JAMA*. 2024;331:49-59. https://doi.org/10.1001/jama.2023.25463
7. Bhurosy T, Niu Z, Heckman CJ. Breastfeeding is possible: a systematic review on the feasibility and challenges of breastfeeding among breast cancer survivors of reproductive age. *Ann Surg Oncol*. 2021;28:3723-3735. https://doi.org/10.1245/s10434-020-09094-1
8. Lambertini M, Di Maio M, Poggio F, et al. Knowledge, attitudes and practice of physicians towards fertility and pregnancy-related issues in young BRCA-mutated breast cancer patients. *Reprod Biomed Online*. 2019;38:835-844. https://doi.org/10.1016/j.rbmo.2018.11.031
9. Tralins AH. Lactation after conservative breast surgery combined with radiation therapy. *Am J Clin Oncol*. 1995;18:40-43. https://doi.org/10.1097/00000421-199502000-00008
10. Moran MS, Colasanto JM, Haffty BG, Wilson LD, Lund MW, Higgins SA. Effects of breast-conserving therapy on lactation after pregnancy. *Cancer J*. 2005;11:399-403. https://doi.org/10.1097/00130404-200509000-00007
11. Sella T, Sorouri K, Rosenberg SM, et al. Breastfeeding experiences among young breast cancer survivors: a survey study. *Cancer*. 2025;131:e35585. https://doi.org/10.1002/cncr.35585
12. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50302 women with breast cancer and 96973 women without the disease. *Lancet*. 2002;360:187-195. https://doi.org/10.1016/S0140-6736(02)09454-0
13. Lambertini M, Santoro L, Del Mastro L, et al. Reproductive behaviors and risk of developing breast cancer according to tumor subtype: a systematic review and meta-analysis of epidemiological studies. *Cancer Treat Rev*. 2016;49:65-76. https://doi.org/10.1016/j.ctrv.2016.07.006
14. Kotsopoulos J, Lubinski J, Salmena L, et al.; Hereditary Breast Cancer Clinical Study Group. Breastfeeding and the risk of breast cancer in BRCA1 and BRCA2 mutation carriers. *Breast Cancer Res*. 2012;14:R42. https://doi.org/10.1186/bcr3138
15. Azim HA, Bellettini G, Liptrott SJ, et al. Breastfeeding in breast cancer survivors: pattern, behaviour and effect on breast cancer outcome. *Breast*. 2010;19:527-531. https://doi.org/10.1016/j.breast.2010.05.018
16. Lambertini M, Kroman N, Ameye L, et al. Long-term safety of pregnancy following breast cancer according to estrogen receptor status. *J Natl Cancer Inst*. 2018;110:426-429. https://doi.org/10.1093/jnci/djx206
17. Sessa C, Balmaña J, Bober SL, et al.; ESMO Guidelines Committee. Risk reduction and screening of cancer in hereditary breast-ovarian cancer syndromes: ESMO Clinical Practice Guideline. *Ann Oncol*. 2023;34:33-47. https://doi.org/10.1016/j.annonc.2022.10.004
18. von Elm E, Altman DG, Egger M, et al.; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet*. 2007;370:1453-1457. https://doi.org/10.1016/S0140-6736(07)61602-X
19. Tolaney SM, Garrett-Mayer E, White J, et al. Updated standardized definitions for efficacy end points (STEEP) in adjuvant

breast cancer clinical trials: STEEP version 2.0. *J Clin Oncol*. 2021;39:2720-2731. https://doi.org/10.1200/JCO.20.03613
20. Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. *J Am Stat Assoc*. 1999;94:496-509. https://doi.org/10.1080/01621459.1999.10474144
21. Gorman JR, Usita PM, Madlensky L, Pierce JP. A qualitative investigation of breast cancer survivors' experiences with breastfeeding. *J Cancer Surviv*. 2009;3:181-191. https://doi.org/10.1007/s11764-009-0089-y
22. Graeser MK, Engel C, Rhiem K, et al. Contralateral breast cancer risk in BRCA1 and BRCA2 mutation carriers. *J Clin Oncol*. 2009;27:5887-5892. https://doi.org/10.1200/JCO.2008.19.9430
23. Tung NM, Boughey JC, Pierce LJ, et al. Management of hereditary breast cancer: American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Surgical Oncology Guideline. *J Clin Oncol*. 2020;38:2080-2106. https://doi.org/10.1200/JCO.20.00299
24. Blondeaux EVA, Sonnenblick A, Agostinetto E, et al. Association between risk-reducing surgeries and survival in young BRCA carriers with breast cancer: an international cohort study. *Lancet Oncol*. 2025;26:759-770. https://doi.org/10.1016/S1470-2045(25)00152-4
25. Johnson HM, Mitchell KB. Breastfeeding and breast cancer: managing lactation in survivors and women with a new diagnosis. *Ann Surg Oncol*. 2019;26:3032-3039. https://doi.org/10.1245/s10434-019-07596-1
26. Helewa M, Lévesque P, Provencher D, et al.; Breast Disease Committee and Executive Committeee and Council, Society of Obstetricians and Gynaecologists of Canada. Breast cancer, pregnancy, and breastfeeding. *J Obstet Gynaecol Can*. 2002;24:164-180; quiz 181–184.
27. Victora CG, Bahl R, Barros AJD, et al.; Lancet Breastfeeding Series Group. Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect. *Lancet*. 2016;387:475-490. https://doi.org/10.1016/S0140-6736(15)01024-7

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