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Long-Term Locoregional Outcomes in a Contemporary Cohort of Young Women With Breast Cancer

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IMPORTANCE Women diagnosed with breast cancer at a young age are felt to have a higher risk for locoregional recurrence (LRR) regardless of type of local therapy.

OBJECTIVE To assess the long-term incidence of isolated LRR by molecular subtype in a modern multicenter cohort of young women.

DESIGN, SETTING, AND PARTICIPANTS This cohort study, a multicenter prospective study named the Young Women's Breast Cancer Study, enrolled 1302 women diagnosed with breast cancer at 40 years or younger from 2006 to 2016. Treatment information and incident LRR (ipsilateral breast/chest or lymph node recurrence) were self-reported on study surveys and confirmed with medical record review; molecular subtype was determined by record review. Analysis was reported from February 2023 to May 2025.

MAIN OUTCOMES AND MEASURES Cumulative incidence of isolated LRR was calculated using the Kaplan-Meier method; hazard ratios were estimated by Cox proportional hazards regression.

RESULTS The cohort included 1135 women with stage I through III breast cancer who had a median follow-up of 10.1 years (range, 0.4-16.3 years). The age at diagnosis was younger than 30 years for 145 patients (12.8%), 31 to 35 years for 318 patients (28.0%), and 36 to 40 years for 672 patients (59.2%). There were 59 isolated local recurrences (5.2%) and 4 isolated regional recurrences (0.4%). Among patients with local therapy and subtype data available (n = 1128), 366 (32%) had luminal A–like tumors; 240 (21%), luminal B–like tumors; 231 (20%) luminal *ERBB2* positive (+)–like (formerly *HER2* positive); 90 (8%) *ERBB2*+-like; and 201 (18%) triple negative. A total of 346 women (30%) had breast-conserving therapy (BCT) (98% of whom had radiation), 296 (26%) unilateral mastectomy, and 487 (43%) bilateral mastectomy. Of women who had mastectomy, 425 (54%) had radiation. The cumulative incidence of LRR at 10.1 years by subtype was as follows: luminal A, 4.4% (range, 1.0%-6.9%); luminal B, 4.7% (range 1.8%-7.7%); luminal *ERBB2*+, 6.1% (range, 3.1%-8.3%); *ERBB2*+, 2.2% (range, 0%-6.3%); and triple negative, 6.5% (range, 4.2%-10.1%). The cumulative incidence of LRR by locoregional treatment type at 10.1 years was 6.7% after BCT (range, 4.3%-10.1%), 6.5% after mastectomy without radiation (range, 0%-7.7%), and 2.4% after mastectomy with radiation (range, 1%-4.2%). Although mastectomy with radiation was associated with the lowest risk of LRR on multivariable analysis, when examined within molecular subtype, there were no differences seen.

CONCLUSIONS AND RELEVANCE In this contemporary cohort of women diagnosed with breast cancer at age 40 years or younger, risk of isolated LRR was relatively low (5.6%) at a median follow-up of 10.1 years, and significant differences were not seen by tumor subtype. Concerns for long-term risk of LRR should not influence surgical decision-making with young women, irrespective of molecular subtype.

Invited Commentary

Supplemental content

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Rates of early-onset breast cancer have been increasing, and breast cancer is now the most common cancer diagnosis in women aged 15 to 39 years.[1] Although distant disease poses the most significant risk, there has been concern about the potential increased risk for isolated locoregional recurrence (LRR) in young patients who do not develop distant disease, with young age having been shown to be an independent risk factor for local recurrence after surgery for breast cancer in some studies.[2,3] Older studies evaluating outcomes in this patient population suggested that although survival was equivalent for young women undergoing breast-conserving therapy (BCT) and mastectomy, local recurrence rates may be higher for women undergoing breast conservation.[4,5] However, more recent studies suggest that young women may have acceptably low rates of local recurrence after breast conservation.[6,7] Recent data also demonstrate that local recurrence risk may be more aligned with breast cancer subtype, rather than surgical procedure, in both young and older women, though studies have been limited by comprehensive availability of biologic subtype.[6,8,9] Studies specifically examining local recurrence risks in young women are further limited by small sample sizes and short follow-up periods.[10-12] A recent meta-analysis noted that data on long-term local recurrence risk for young women with breast cancer were insufficient to make conclusive statements regarding risk of local recurrence after breast conservation for this population.[13]

Data from prior studies evaluating risk of local recurrence are further hampered by limited use of modern systemic therapy (particularly *ERBB2*-directed treatment [formerly *HER2*]) during the time frame of the study. It is well recognized that optimal systemic therapy significantly reduces the risk for LRR.[14,15] Additionally, indications for postmastectomy radiation have expanded over time, and radiation planning, particularly for young women undergoing BCT, has included a boost dose to maximally reduce risk for local recurrence in recent years.[16-18] Thus, contemporary cohorts inclusive of young women who have received optimal systemic and local therapy can provide LRR estimates that account for modern treatment. We sought to evaluate rates of isolated LRR within molecular subtype by local regional treatment type among women diagnosed at 40 years and younger who were treated with modern systemic therapy for stage I through III breast cancer and followed up prospectively as part of a multicenter longitudinal cohort study. In addition, we also assessed factors predictive of overall LRR in this cohort.

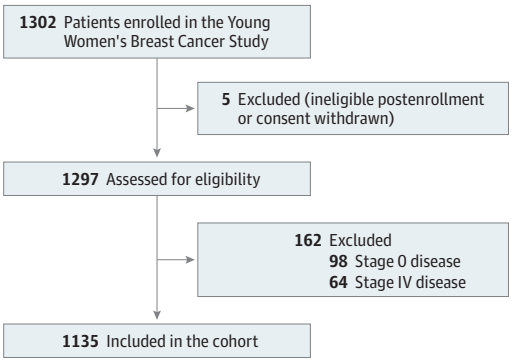
Key Points

Question Does contemporary risk for isolated locoregional recurrence (LRR) in young women with breast cancer vary by molecular subtype?

Findings In this cohort study including 1135 women, risk for isolated LRR was 5.6% at a median follow-up of 10.1 years, and no significant differences were seen based on type of surgery or molecular subtype.

Meaning Concerns for long-term risk of LRR should not impact surgical decision-making with young women, irrespective of molecular subtype.

Figure 1. Study Flow Diagram



Methods

Study Design and Population

The Young Women's Breast Cancer Study (YWS) is a multicenter, prospective cohort study established to examine biological, medical, and quality-of-life issues in women 40 years or younger diagnosed with primary invasive breast cancer or ductal carcinoma in situ. Participating hospitals included both academic and community centers in Massachusetts, Toronto, Canada, Colorado, and Minnesota. Over 10 years (October 10, 2006, to June 30, 2016), 2162 eligible women were identified through pathology record review or review of clinic lists at participating hospitals and were invited to participate. A total of 1302 patients provided written informed consent, although 4 were found to be ineligible and 1 withdrew consent after enrollment. Participants were sent a survey at study baseline followed by additional surveys twice a year for the first 3 years after diagnosis and annually thereafter. The YWS is approved by the institutional review board at the Dana-Farber Harvard Cancer Center and other participating sites. Study design details were published previously.[19]

Patient, Disease, and Treatment Characteristics

For this analysis, we included patients with stage I through III breast cancer and excluded patients with stage 0 or stage IV disease at diagnosis. Patient characteristics were collected through the baseline survey or through medical record review, including race, ethnicity, and marital status. For baseline survey nonresponders or instances where this information was not reported, race and ethnicity as determined from medical record at enrollment were used. Pathology and medical records of patients were reviewed for disease staging, genetic testing and result if available, tumor hormone receptor status, and *ERBB2* status (formerly *HER2*). We constructed molecular subtype as follows: luminal A (hormone receptor [HR] positive, *ERBB2* negative, grade 1/2), luminal B (HR positive, *ERBB2* negative, grade 3), luminal *ERBB2* positive (+) (HR+, *ERBB2*+), *ERBB2*+ enriched (HR negative,

Table 1. Patient and Treatment Characteristics for 1135 Women Diagnosed at Age 40 Years or Younger With Breast Cancer (2006-2016)

Characteristic	No. (%)
Age at diagnosis, y	
≤30	145 (12.8)
31-35	318 (28.0)
36-40	672 (59.2)
Race[a]	
American Indian or Alaskan Native	4 (0.4)
Asian	82 (7.2)
Black, Haitian, or African American	37 (3.3)
White	959 (84.5)
Unknown	38 (3.4)
Multiracial	15 (1.3)
Hispanic ethnicity[a]	
Yes	50 (4.4)
No	908 (80.0)
Unknown	177 (15.6)
Marital status	
Married or living as married	696 (61.3)
Single, divorced, or widowed	226 (19.9)
Missing	213 (18.8)
Tumor stage	
T1	563 (49.6)
T2	435 (38.3)
T3	120 (10.6)
T4	15 (1.3)
Tis	2 (0.2)
Pathologic node stage	
N0	617 (54.4)
N1	383 (33.7)
N2	92 (8.1)
N3	39 (3.4)
X	4 (0.4)
Overall stage	
I	413 (36.4)
II	525 (46.3)
III	197 (17.4)
Grade	
Low	74 (6.5)
Intermediate	383 (33.7)
High	670 (59.0)
Missing	8 (0.7)
Genetic testing	
*BRCA*1/2 pathogenic variant positive	131 (11.5)
BRCA negative/VUS	850 (74.9)
Not tested	154 (13.6)
Biologic subtype[b]	
Luminal A	366 (32.2)
Luminal B	240 (21.1)
Luminal *ERBB2*+	231 (20.4)
ERBB2+	90 (7.9)
Triple negative	201 (17.7)
Missing	7 (0.6)
Chemotherapy	
Neoadjuvant	319 (28.1)
Adjuvant	614 (54.1)
None	166 (14.6)
Unknown	36 (3.2)
Endocrine therapy received (by patients HR+)	
Yes	619 (75.8)
No	69 (8.4)
Missing	129 (15.8)
Surgery/radiation	
BCT[c]	346 (30.5)
Unilateral mastectomy and PMRT	186 (16.4)
Unilateral mastectomy without PMRT	110 (9.7)
Bilateral mastectomy and PMRT	239 (21.1)
Bilateral mastectomy without PMRT	248 (21.9)
Missing	6 (0.5)
Axillary surgery	
Sentinel node biopsy only	602 (53.0)
Axillary lymph node dissection[d]	524 (46.2)
No nodal surgery	2 (0.2)
Missing	7 (0.6)

Abbreviations: +, positive; BCT, breast-conserving therapy; HR, hormone receptor; PMRT, postmastectomy radiation therapy; Tis, tumor in situ; VUS, variant of uncertain significance; X, unknown; nodes could not be or were not surgically evaluated.

[a] Race and ethnicity data were collected through the baseline survey or determined from medical record at enrollment.

[b] We constructed molecular subtype as follows: luminal A (HR positive, *ERBB2* negative, grade 1/2), luminal B (HR positive, *ERBB2* negative, grade 3), luminal *ERBB2* positive (+) (HR+, *ERBB2*+), *ERBB2*+ enriched (HR negative, *ERBB2*+), and triple negative (HR negative, *ERBB2* negative).

[c] Including 7 patients (2%) who did not have radiation.

[d] With or without sentinel node biopsy.

ERBB2+), and triple negative (HR negative, *ERBB2* negative). Surgery, chemotherapy, and radiotherapy information (yes/no) was obtained by a combination of self-report and medical record review. Given the very small number of patients who received lumpectomy without radiation (n = 7), these patients were all classified as having BCT. Endocrine therapy use was based on self-report of any use from the baseline, 6-month, or 1-year survey.

Ascertainment of Recurrence

Information about recurrence, including site and date, was obtained by self-report on follow-up surveys and confirmed by medical record review. For patients who were not responding to study surveys and/or deemed lost to follow-up, medical records were reviewed at 10 years postdiagnosis to ascertain recurrence status. The current analysis includes events ascertained through January 31, 2023. Collectively referred to as LRR, local recurrence was classified as disease in the ipsilateral breast or chest, and regional recurrence was classified as

Table 2. Five- and 10-Year Cumulative Incidence of Locoregional Recurrence by Subtype and Locoregional Treatment Strategy[a]

Strategy	Luminal A		Luminal B		Luminal *ERBB2*+		*ERBB2*+		Triple negative	
	Events, No./No. of patients (cumulative LRR, %)	*P* value	Events, No./No. of patients (cumulative LRR, %)	*P* value	Events, No./No. of patients (cumulative LRR, %)	*P* value	Events, No./No. of patients (cumulative LRR, %)	*P* value	Events, No./No. of patients (cumulative LRR, %)	*P* value
5 y										
Breast-conserving therapy	1/138 (0.7)	.16	2/61 (3.3)	.18	3/60 (5.0)	.60	0/16	>.99	4/69 (5.8)	.54
Mastectomy without radiation	4/130 (3.1)		5/65 (7.7)		3/73 (4.1)		0/26		1/60 (1.7)	
Mastectomy and radiation	0/98		2/110 (1.8)		2/97 (2.1)		1/48 (2.1)		3/71 (4.2)	
Overall rates	5/366 (1.4)		9/236 (3.8)		8/230 (3.5)		1/90 (1.1)		8/200 (4.0)	
10 y										
Breast-conserving therapy	6/138 (4.3)	.09	4/61 (6.6)	.14	5/60 (8.3)	.26	1/16 (6.3)	.41	7/69 (10.1)	.37
Mastectomy without radiation	9/130 (6.9)		5/65 (7.7)		6/73 (8.2)		0/26		3/60 (5.0)	
Mastectomy and radiation	1/98 (1.0)		2/110 (1.8)		3/97 (3.1)		1/48 (2.1)		3/71 (4.2)	
Overall rates	16/366 (4.4)		11/236 (4.7)		14/230 (6.1)		2/90 (2.2)		13/200 (6.5)	

Abbreviations: HR, hormone receptor; LRR, locoregional recurrence.

[a] We constructed molecular subtype as follows: luminal A (HR positive, *ERBB2* negative, grade 1/2), luminal B (HR positive, *ERBB2* negative, grade 3), luminal *ERBB2* positive (+) (HR+, *ERBB2*+), *ERBB2*+ enriched (HR negative, *ERBB2*+), and triple negative (HR negative, *ERBB2* negative).

disease in the ipsilateral axillary, internal mammary, or supraclavicular lymph nodes. As there is often difficulty in classifying ipsilateral disease as a recurrence vs a new primary breast cancer, we classified any disease of the ipsilateral breast as local recurrence. Patients with distant recurrence and LRR identified concurrently (ie, dates were ≤3 months apart) were grouped for this analysis as having distant recurrence rather than LRR, as the presence of distant recurrence makes a LRR less clinically meaningful.

Statistical Analysis

Frequencies and proportions were calculated for patient characteristics, clinicopathologic features, and treatment characteristics. Overall and 5-year cumulative incidence LRR were estimated by subtype and compared within each subtype group by locoregional treatment strategy (BCT, mastectomy with radiation, and mastectomy without radiation). A competing risk analysis was conducted with locoregional event considered as the event of interest and distant recurrence (including concomitant locoregional and distant recurrence) considered as the competing event. Cox proportional hazard regression models evaluated factors associated with LRR risk. Analyses were conducted using SAS version 9.4 (SAS Institute).

Results

Patient, Tumor, and Treatment Characteristics

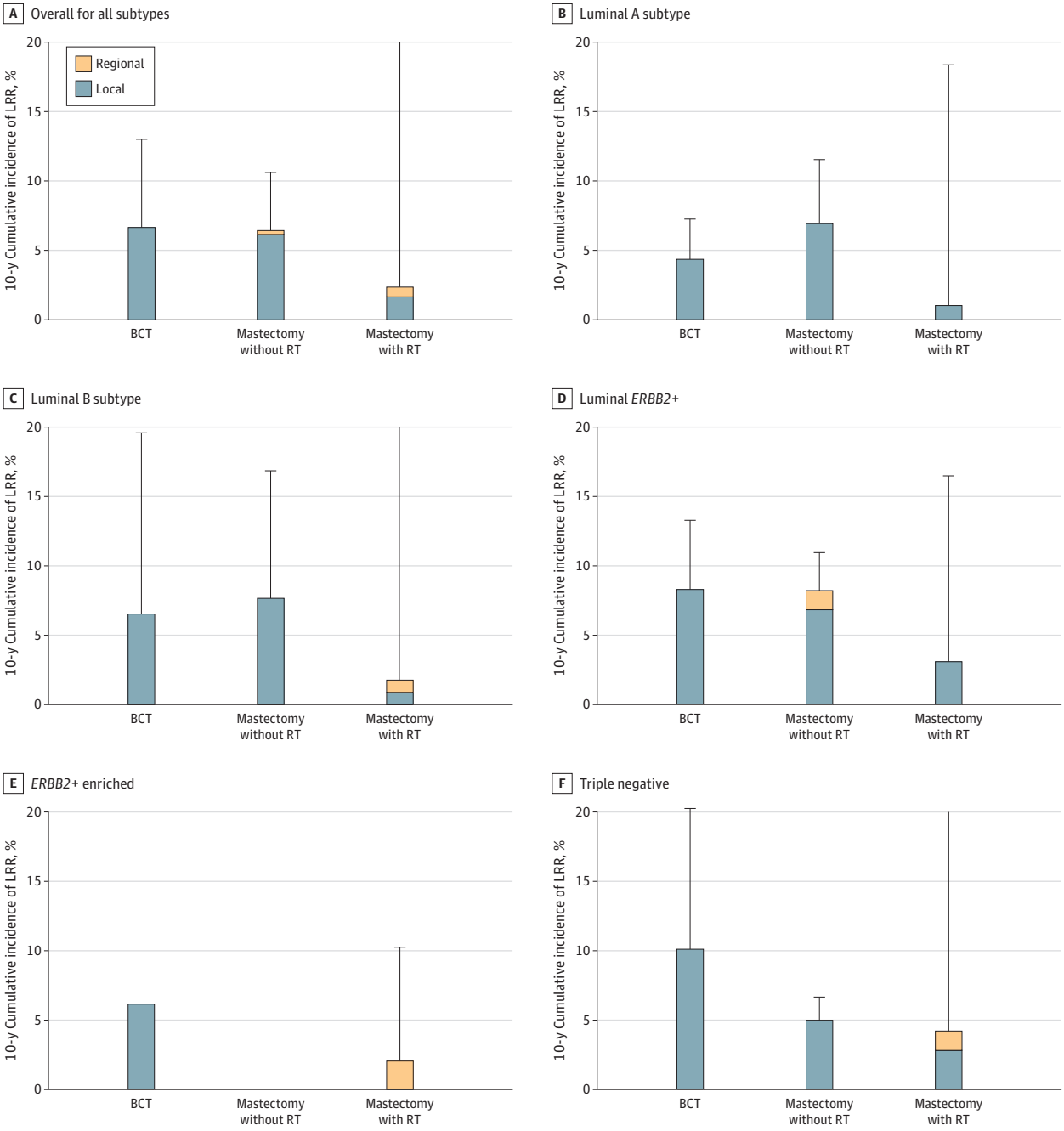
After excluding 98 patients with stage 0 disease and 64 patients with stage IV disease, there were 1135 evaluable patients (**Figure 1**). The median length of follow-up from diagnosis was 10.1 years (range, 0.4-16.3 years). Patient characteristics are described in **Table 1**. The distribution of age at diagnosis was as follows: 145 were younger than 30 years (12.8%), 318 were aged 31 to 35 years (28.0%), and 672 were aged 36 to 40 years (59.2%). Most patients were White (n = 959, 84.5%) and married or partnered (n = 696, 61.3%).

Clinical and pathologic features are described in Table 1. Most patients (n = 981, 86.4%) had genetic testing, with 131 (11.5%) reporting testing positive for a pathogenic variant. Most patients had stage I or II breast cancer (n = 938, 82.7%), and molecular subtypes included the following: 366 patients (32.2%) had luminal A, 240 patients had (21.1%) luminal B, 231 patients (20.4%) had luminal *ERBB2*+, 90 patients (7.9%) had *ERBB2*+, and 201 (17.7%) had triple negative. Treatment characteristics are presented in Table 1. Most patients received chemotherapy, with 319 (28.1%) receiving neoadjuvant chemotherapy and 614 (54.1%) receiving adjuvant chemotherapy. For patients with *ERBB2*+ tumors, 296 (92.2%) received *ERBB2*-directed therapy, (213 [92.2%] patients with luminal *ERBB2*+ cancers and 83 [92.2%] patients with *ERBB2*+ cancers). For patients with HR+ breast cancer, 619 (75.8%) reported endocrine therapy use in the first year of follow-up. Regarding local therapy, 346 patients (30.5%) had BCT (n = 7 [2%] in this group did not receive radiation); 110 (9.7%) had unilateral mastectomy without radiation, 248 (21.9%) had bilateral mastectomy without radiation, and 186 patients (16.4%) and 239 patients (21.1%) had unilateral and bilateral mastectomy with radiation, respectively. Almost all patients had lymph node surgery: 602 patients (53.0%) had sentinel lymph node biopsy only and 524 patients (46.2%) had axillary lymph node dissection (with or without sentinel node evaluation).

Overall Risk of Recurrence

At a median follow-up of 10.1 years (range, 0.4-16.3 years), 63 patients (5.6%) experienced an isolated LRR, including local recurrence in 59 patients (5.2%) and regional recurrence in 4 (0.4%) patients. Over the entire follow-up period, distant disease was seen in 130 patients (11.5%), including 51 patients (4.5%) who had concomitant LRR.

Figure 2. Cumulative Incidence of Locoregional Recurrence (LRR) at 10 Years



We constructed molecular subtypes as follows: luminal A (hormone receptor [HR] positive, *ERBB2* negative, grade 1/2), luminal B (HR positive, *ERBB2* negative, grade 3), luminal *ERBB2* positive (+) (HR+, *ERBB2*+), *ERBB2*+ enriched (HR negative, *ERBB2*+), and triple negative (HR negative, *ERBB2* negative). BCT indicates breast-conserving therapy; RT, radiation therapy.

Locoregional Risk by Biologic Subtype and Locoregional Treatment

At 5 years, the cumulative incidence of isolated LRR (without concomitant systemic recurrence) by tumor subtype was: luminal A, 1.4% (range, 0%-3.1%); luminal B, 3.8% (range 1.8%-7.7%); luminal *ERBB2*+, 3.5% (range, 2.1%-5.0%); *ERBB2*+, 1.1% (range, 0%-2.1%); and triple negative, 4.0% (range, 1.7%-5.8%). The cumulative incidence of LRR at 5 years by locoregional treatment type was 2.9% after BCT (range, 0%-5.8%), 3.7% after mastectomy without radiation (range, 0%-7.7%), and 1.9% after mastectomy with radiation (range, 0%-4.2%). There were no significant differences associated with locoregional treatment type within molecular subtype (**Table 2** and eFigures 1-6 in Supplement 1).

Table 3. Multivariate Analysis of Factors Impacting Risk for Locoregional Recurrence (Patients With Distant Disease Excluded) in Women Diagnosed at Age 40 Years or Younger With Breast Cancer (2006-2016)

Factor	Hazard ratio (95% CI)	*P* value
Age, y		
≤30	1.06 (0.50-2.28)	.88
31-35	1.11 (0.62-1.98)	.72
36-40	1 [Reference]	
Subtype[a]		
Luminal A	1 [Reference]	
Luminal B	1.21 (0.54-2.71)	.65
Luminal *ERBB2*+	1.51 (0.70-3.25)	.29
ERBB2+	0.48 (0.11-2.09)	.33
Triple negative	1.38 (0.61-3.16)	.44
Chemotherapy		
No	1 [Reference]	
Yes, neoadjuvant	1.49 (0.51-4.35)	.46
Yes, adjuvant	1.00 (0.42-2.34)	.99
Local therapy		
BCT	1 [Reference]	
Mastectomy without RT	0.85 (0.48-1.50)	.57
Mastectomy with RT	0.27 (0.13-0.59)	.001
Stage		
I	1 [Reference]	
II	0.74 (0.39-1.42)	.37
III	1.17 (0.44-3.09)	.75

Abbreviations: BCT, breast-conserving therapy; RT, radiation therapy.

[a] We constructed molecular subtype as follows: luminal A (HR positive, *ERBB2* negative, grade 1/2), luminal B (HR positive, *ERBB2* negative, grade 3), luminal *ERBB2* positive (+) (HR+, *ERBB2*+), *ERBB2*+ enriched (HR negative, *ERBB2*+), and triple negative (HR negative, *ERBB2* negative).

At 10.1 years, the cumulative incidence of LRR by subtype was luminal A, 4.4% (range, 1.0%-6.9%); luminal B, 4.7% (range, 1.8%-7.7%); luminal *ERBB2*+, 6.1% (range, 3.1%-8.3%); *ERBB2*+, 2.2% (range, 0%-6.3%); and triple negative, 6.5% (range, 4.2%-10.1%). The cumulative incidence of LRR by locoregional treatment type at 10.1 years was 6.7% after BCT (range, 4.3%-10.1%), 6.5% after mastectomy without radiation (range, 0%-7.7%), and 2.4% after mastectomy with radiation (range, 1%-4.2%). There were no significant differences associated with locoregional treatment type within molecular subtype (Table 2 and **Figure 2**). In patients with triple-negative breast cancers (n = 201), there were 5 patients who had local recurrences recorded after 5 years, 3 after breast conservation, and 2 after mastectomy without radiation. On review of these cases, none of these recurrences were triple negative and likely represented a new primary breast cancer.

In the multivariate model (**Table 3**), isolated LRR risk did not differ by subtype. Only treatment with mastectomy and radiation (vs BCT) was associated with a lower risk for LRR (hazard ratio, 0.27; 95% CI, 0.13-0.59). Age, chemotherapy (neoadjuvant or adjuvant), and stage were also not associated with LRR risk.

Discussion

Among more than 1100 women diagnosed with breast cancer at 40 years and younger followed up prospectively, we observed overall low rates of isolated LRR at a median follow-up of 10.1 years. In our data, we did not observe significant differences in LRR based on type of locoregional treatment within each tumor subtype category, which is consistent with other studies.[20,21] Acknowledging the likely contribution of inappropriate patient selection for surgery, for those women with early breast cancer who underwent BCT or mastectomy without radiation, no differences were seen. Although young age has historically been associated with higher risk for local recurrence, the rates of LRR we observed were comparable with rates observed in contemporary studies inclusive of women of all ages.[13,22] In the POSH cohort study, which enrolled more than 3000 women diagnosed with breast cancer in the United Kingdom at age 18 to 40 years, women had higher rates of local recurrence at 10 years than those seen in our study (11.68% and 4.93% after breast conservation and mastectomy, respectively, compared with 6.2% and 4.2%). However, patients in our study were more likely to receive neoadjuvant chemotherapy (28.1% vs 15.5%, respectively) and more likely to receive *ERBB2*-directed therapy (92.2% vs 12.5%, respectively), largely reflecting the periods of enrollment of the 2 studies, and also more likely to receive endocrine therapy (75.8% vs 65.3%, respectively). Thus, contemporary treatment practices for systemic therapy likely contributed to the lower rates of local recurrence in our study (2006-2016 vs 2000-2008 for POSH).[7]

We observed the numerically lowest rates of local recurrence among women with *ERBB2*+ disease, supporting findings from recent studies that have assessed the impact of *ERBB2*-directed therapy on local recurrence rates in patients of all ages.[15] Vuong et al[23] evaluated breast cancer treatment outcomes for 1431 patients diagnosed at 40 years and younger and demonstrated a numerically higher incidence of any recurrence for patients with estrogen receptor (ER)–negative/*ERBB2*+ and triple-negative breast cancers at 10 years, although their study did not differentiate between locoregional and distant recurrences and noted that, in fact, most recurrences were distant. While 90% of patients with *ERBB2*+ breast cancers in their cohort received *ERBB2*-directed therapy, which was similar to the 92.2% in our study, fewer patients in the study by Vuong et al[23] received neoadjuvant chemotherapy (18.5% vs 28.1% in our study).[23] We also observed additional LR events in patients with triple-negative breast cancers between 5 and even 10 years, with 5 new estrogen-sensitive breast cancers diagnosed at least 5 years after the primary triple-negative cancer diagnosis, likely indicative of a new primary breast cancer.[24]

There were numeric but not statistically significant increases in local recurrences at 10 years vs 5 years among women with luminal A, luminal B, and luminal *ERBB2*+ breast cancers, which is consistent with other studies

demonstrating late recurrences associated with younger age at diagnosis and ER-positive disease.[25] Previous work has demonstrated luminal breast cancer subtypes are associated with poorer survival in young women.[26,27] It is suggested that these outcomes are attributed in part to biologic differences related to estrogen-sensitive breast cancers in young women and to potential for decreased efficacy and adherence to endocrine therapy in these patients.[28,29] As previously noted, effective systemic therapy contributes significantly to optimal local control, and efforts to support adherence to endocrine therapy among young women with hormone-sensitive breast cancer is essential.[30,31]

While patients receiving mastectomy with radiation had the numerically lowest rates of local recurrence in our study, and receipt of postmastectomy radiation was associated with decreased risk for LRR in the multivariable analysis, this is confounded by the fact that this is a higher-risk group more likely to have a distant recurrence (and therefore censored as part of the current analysis), resulting in a smaller number of patients who are recommended for postmastectomy radiation and ultimately are at risk for an isolated local recurrence. We elected to focus our study design on a group of patients who did not develop distant disease, where an isolated local recurrence would be an impactful event. Contemporary recommendations for postmastectomy radiation have expanded, particularly for younger patients, but the benefits must be weighed against the potential morbidity of radiation and negative impact on quality of life.[32,33]

Limitations

Our study should be interpreted in the context of some limitations. Most study participants were White and non-Hispanic, with earlier stage disease. As we sought to identify if there were differences in incidence of local recurrence in those patients for whom local recurrence would be a highly clinically meaningful event (ie, those patients without metastatic disease), the possibility of selection bias cannot be excluded, particularly among those who had mastectomy with radiation, as they represent a select group of patients with higher-risk disease who were excellent responders and did not develop metastatic disease. Overall, the number of local recurrences was small, so subset analysis may have been underpowered to detect statistically significant differences.

Conclusions

Reassuringly, in this large contemporary study of women diagnosed with breast cancer at age 40 years and undertreated with modern local and systemic therapy, we observed overall low rates of isolated LRR in long-term follow-up, with no significant differences by local therapy strategy when compared within tumor subtype. Given the lengthy survivorship period for young women with breast cancer and increased numbers of young women being diagnosed, even longer-term follow-up is critical for understanding future LRR risk in these patients. Continued follow-up of this cohort will further inform risk of LRR, particularly in those patients with hormone-sensitive disease.

ARTICLE INFORMATION

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