Original Article

Breast Conservation Among Older Patients With Early-Stage Breast Cancer: Locoregional Recurrence Following Adjuvant Radiation or Hormonal Therapy

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BACKGROUND: For patients with breast cancer undergoing breast-conserving surgery (BCS), adjuvant radiation (RT) and hormonal therapy (HT) reduce the risk of locoregional recurrence (LRR). Although several studies have evaluated adjuvant HT ± RT, the outcomes of HT versus RT monotherapy remain less clear. In this study, the risk of LRR is characterized among older patients with early-stage breast cancer following adjuvant RT alone, HT alone, neither, or both. **METHODS:** This study included female patients from the Memorial Sloan Kettering Cancer Center (New York, New York) who were aged ≥65 years with estrogen receptor–positive (ER+)/human epidermal growth factor receptor 2–negative (HER2–) T1N0 breast cancer treated with BCS. The primary endpoint was time to LRR evaluated by Cox regression analysis. **RESULTS:** There were 888 women evaluated with a median age of 71 years (range, 65-100 years) and median follow-up of 4.9 years (range, 0.0-9.5 years). There were 27 LRR events (3.0%). Five-year LRR was 11% for those receiving no adjuvant treatment, 3% for HT alone, 4% for RT alone, and 1% for HT and RT. LRR rates were significantly different between the groups ($P < .001$). Compared with neither HT nor RT, HT or RT monotherapy each yielded similar LRR reductions: HT alone (HR, 0.27; 95% CI, 0.10-0.68; $P = .006$) and RT alone (HR, 0.32; 95% CI, 0.11-0.92; $P = .034$). Distant recurrence and breast cancer–specific survival rates did not significantly differ between groups. **CONCLUSIONS:** LRR risk following BCS is low among women aged ≥65 years with T1N0, ER+/HER2– breast cancer. Adjuvant RT and HT monotherapy each similarly reduce this risk; the combination yields a marginal improvement. Further study is needed to elucidate whether appropriate patients may feasibly receive adjuvant RT monotherapy versus the current standards of HT monotherapy or combined RT/HT. ***Cancer* 2021;127:1749-1757**. *© 2021 American Cancer Society*.

KEYWORDS: breast cancer, breast cancer–specific survival, breast-conserving surgery, hormonal therapy, locoregional recurrence, radiation therapy.

INTRODUCTION

Of 276,480 new cases of invasive breast cancer expected to be diagnosed among American women in 2020, approximately 35% will arise in those over 65 years of age.[1,2] With the greater incidence of comorbidities and competing risks in older patients, treatment decisions for those with estrogen receptor–positive (ER+) early-stage disease should not be guided solely by chronological age but must balance health status, life expectancy, individual preferences, and sustained quality of life.[3]

Adjuvant radiation therapy (RT) improves local control and survival outcomes following breast-conserving surgery (BCS) for invasive breast cancer.[4-6] A large body of literature shows that adjuvant hormonal therapy (HT), such as selective estrogen-receptor modulators and aromatase inhibitors, further reduces local recurrence, distant metastases, and mortality among broadly selected cohorts of patients with breast cancer.[7,8] Thus, following BCS, adjuvant RT and HT represent the standard of care for all stages of ER+ breast cancer.

Although effective and well-tolerated, RT can be time-consuming, resource intensive, and inconvenient. In addition, RT carries risks of morbidity, including adverse cosmesis, dermatitis, breast pain, cardiopulmonary toxicity, and the rare risk of secondary malignancy. HT similarly poses challenges, including limited long-term adherence and the risks of thromboembolic disease, gynecologic malignancies, osteoporosis, fracture, myalgias, and arthralgias, which can

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be problematic in older populations. In an effort to optimize oncologic outcomes while limiting toxicity, several studies have shown that omission of RT in the setting of prolonged HT use among certain subgroups maintains excellent disease-specific survival without significantly compromising local control.[9-14]

Although omission of RT in the setting of HT has been extensively studied, there are limited data to support the omission of HT among those who opt to receive RT.[15-17] The NSABP (National Surgical Adjuvant Breast and Bowel Project) B-21 study addressed whether tamoxifen with breast RT was more effective than either modality alone among a cohort consisting of all age groups and without universal receptor profiling. The study found that in-breast recurrence at a follow-up of 8 years was lowest among those who received dual therapy with RT and HT (9.3% RT; 16.5% HT; 2.8% RT + HT), with no significant survival differences between groups. Although B-21 included only tumors <1 cm, 12% were estrogen receptor–negative (ER–), and 30% had unknown ER status.[18] Thus, with current clinicopathologic classification schemes to identify favorable-risk older patients with early-stage ER+ breast cancer, it remains unclear whether it is feasible to omit HT in the setting of adjuvant RT without compromising local recurrence, distant metastasis, or survival outcomes.

MATERIALS AND METHODS

Study Population

Upon Memorial Sloan Kettering Cancer Center Institutional Review Board approval, eligible patients were identified from a prospectively maintained institutional database. Patients were included if they were women ≥65 years of age with T1 (<20 mm), N0, ER+, human epidermal growth factor receptor 2–negative (HER2–) tumors who underwent BCS from 2010 to 2015. ER+ was defined as >1% staining by immunohistochemistry. A Suemoto index (SI) was calculated for each patient as a measure of overall health status. The index derives 10-year mortality risk among community-dwelling older adults based on a validated model incorporating age, comorbidities, physical activity level, cognitive status, and alcohol or tobacco use.[19] Patients were excluded if they had a prior cancer diagnosis or bilateral breast cancer or if they had received any chemotherapy.

Relevant clinicopathologic parameters were collected, including age, tumor size, overall tumor grade, lymphovascular invasion (LVI), and Oncotype Dx Recurrence score (RS; Genomic Health, Redwood City, California). Treatment data were also evaluated, including type of axillary surgery, receipt of RT and modality, the use of RT boost, and HT use and adherence.

Patients were classified into 4 distinct groups based on the use of RT and HT: RT monotherapy, HT monotherapy, RT and HT, or neither. Those in the adjuvant RT monotherapy group did not receive any HT (ie, this group excludes those who halted HT prematurely). Those classified as receiving HT had completed the full course as recommended by the treating physician or were fully compliant at the time of their last follow-up.

Statistical Analysis

The primary outcome of interest was locoregional recurrence (LRR), defined as the time from surgery to first recurrence in the ipsilateral breast and/or lymph nodes. If the patient had multiple re-excisions, the time from last surgery was used. Recurrence was defined as the identification of invasive or in situ breast cancer in the previously treated breast or ipsilateral lymph nodes ≥30 days after surgery for the primary breast cancer. Secondary endpoints included distant recurrence (DR), overall survival (OS), and breast cancer–specific survival (BCSS). Patient and treatment characteristics were summarized using median and range for continuous variables and counts for categorical variables. Histopathologic characteristics were compared using the chi-square test or Fisher's test for categorical variables and Wilcoxon rank sum test or *t* test for continuous variables. A multivariable Cox regression model was then constructed using age, SI, tumor histology, size, grade, Oncotype Dx RS, LVI, treatment group, and treatment by SI interaction as the covariates of interest (determined a priori), and clinical outcome (recurrence or death) as the dependent variable of interest. An initial exploratory analysis showed that SI was significantly different between the treatment groups. Based on this finding and in consideration of the clinical relevance of comorbidity (SI) in this older cohort of individuals, we postulated that SI may work as an effect modifier (with treatment) in determining survival. Therefore, we included an interaction term between SI and treatment in the Cox regression model. Covariates that were not significant at a type I error rate of 0.05 were eliminated from the model using backward elimination. All statistical analyses were conducted with a type I error rate (α) of 0.05 and were performed using R version 3.4.1 (R Core Development Team, Vienna, Austria).

TABLE 1. Patient and Treatment Characteristics

	Clinicopathologic Characteristics by Treatment Quartile										
	All Patients (n = 888)		RT Only (n = 118)		HT Only (n = 233)		RT + HT (n = 398)		Neither RT or HT (n = 134)		
Characteristic	No.	%	No.	%	No.	%	No.	%	No.	%	*P*[a]
Age, y											
Age ≥70	536	60.4	58	49.2	190	81.5	166	41.7	117	87.3	<.001[b]
Median (range)	71 (65-100)		69 (65-80)		75 (65-100)		69 (65-86)		76 (65-94)		<.001[b]
Mean (SD)	72 (5.7)		70 (3.5)		75 (5.7)		70 (4.2)		76 (6.1)		
Suemoto index											
Median (range)	30 (12-98)		28 (12-81)		43 (16-98)		27 (14-96)		43 (17-98)		<.001[b]
Mean (SD)	37 (19)		30 (12)		45 (20)		30 (14)		49 (21)		
Tumor size											
Median (range)	1.0 (0.1-2.0)		1.0 (0.1-2.0)		0.9 (0.1-2.0)		1.0 (0.1-2.0)		1.0 (0.1-2.0)		.835
Mean (SD)	1.0 (0.5)		1.0 (0.5)		1.0 (0.5)		1.0 (0.5)		1.0 (0.5)		
Histology											
Invasive ductal	681	76.7	88	74.6	175	75.1	310	77.9	105	78.4	.067
Invasive lobular	109	12.3	12	10.2	31	13.3	52	13.1	13	9.7	
Invasive ductal and lobular	51	5.7	11	9.3	8	3.4	25	6.3	7	5.2	
Other	47	5.3	7	5.9	19	8.2	11	2.8	9	6.7	
Overall tumor grade											
Grade 1	337	38.0	49	41.5	92	39.5	140	35.2	54	40.3	.489
Grade 2	507	57.0	65	55.1	127	54.5	241	60.6	71	53.0	
Grade 3	44	5.0	4	3.4	14	6.0	17	4.2	9	6.7	
Lymphovascular invasion											
Identified	86	9.7	13	11.0	17	7.3	44	11.1	12	9.0	.444
Not identified	718	80.9	93	78.8	196	84.1	320	80.4	105	78.4	
Suspicious	21	2.4	2	1.7	5	2.1	7	1.7	7	5.2	
Unknown	63	7.1	10	8.5	15	6.4	27	6.8	10	7.5	
Axillary surgery											
Sentinel node biopsy	799	90.0	114	96.6	195	83.7	385	96.7	101	75.4	<.001[b]
None	89	10.0	4	3.4	38	16.3	13	3.3	33	24.6	
Oncotype Dx											
Recurrence score >25	6	0.7	1	0.8	2	0.9	1	0.3	2	1.5	.465
Median (range)	13.0 (0-39)		14 (3-30)		14 (0-29)		13 (0-39)		16 (4-39)		
Mean (SD)	13.6 (6.5)		14.6 (7.2)		14.4 (6.1)		12.5 (6.1)		17.6 (7.8)		.007[b]
Recurrence score available											
Available	233	26.2	39	33.1	43	18.5	133	33.4	18	13.4	<.001[b]
Unavailable	655	73.8	79	66.9	190	81.5	265	66.6	116	86.6	
Radiation therapy	516	58.1									
Conventional whole breast	77	14.9	14	11.9	-	-	63	15.8	-	-	.497
Hypofractionated whole breast	265	51.4	63	53.4	-	-	202	50.8	-	-	
Partial breast	54	10.4	15	12.7	-	-	39	9.8	-	-	
Unknown modality	120	23.3	26	22.0	-	-	94	23.6	-	-	
Boost											
Yes	227	44.0	52	44.1	-	-	175	44.0	-	-	.913
No	174	33.7	40	33.9	-	-	134	33.7	-	-	
Unknown	115	22.3	26	22.0	-	-	89	22.3	-	-	

Abbreviations: HT, hormonal therapy; RT, radiation therapy.
[a]*P* values are statistically significant.
[b]Comparison of groups by χ^2 test for categoric variables.

RESULTS

Patient Population and Clinicopathologic Characteristics

The study cohort included 888 women aged ≥65 years with ER+/HER2– T1N0 breast cancer, who underwent BCS between 2010 and 2015 with a median follow-up of 4.9 years (range, 0.0-9.5 years). Clinicopathologic characteristics were similar among the 4 treatment groups (RT, HT, neither, or both) with regards to tumor size, histology, tumor grade, LVI, and high Oncotype DX RS (Table 1). Median age at time of BCS was 71 years (range, 65-100 years), median tumor size was 1.0 cm (range, 0.1-2.0 cm), and the most common histology was invasive ductal carcinoma (n = 681, 76.7%). Most tumors were grade 2 (n = 507, 57.1%) and did not exhibit LVI (n = 718, 80.9%).

Median overall SI was 30 (range, 12-98), with the greatest comorbidity burden in the no-adjuvant-treatment

TABLE 2. Recurrence and Death Rates

	Disease Recurrence or Death									
	All Patients (n = 888)		RT only (n = 118)		HT only (n = 233)		RT + HT (n = 398)		Neither RT or HT (n = 134)	
Event	No.	%	No.	%	No.	%	No.	%	No.	%
Locoregional recurrence	27	3.0	5	4.2	7	3.0	3	0.8	12	9.0
Local (in breast) only	24	2.7	5	4.2	6	2.6	1	0.3	12	9.0
Regional only	2	0.2	0	0.0	1	0.4	1	0.3	0	0.0
Local and regional	1	0.1	0	0.0	0	0.0	1	0.3	0	0.0
Distant recurrence	11	1.2	4	3	1	0.4	3	0.8	3	2.2
Death[a]	65	7.3	10	8.5	16	6.9	18	4.5	20	14.9
Breast cancer	3	0.3	1	0.8	0	0.0	1	0.3	1	0.7
Other	62	7.0	9	7.6	16	6.9	18	4.5	19	14.2

Abbreviations: HT, hormonal therapy; RT, radiation therapy.
[a]One patient is included in the total number of patients who died during follow-up (N = 65) but is not included in the adjuvant treatment group stratified columns nor included in the analysis given inadequate documentation after surgery to determine adjuvant treatment group.

(43; range, 17-98) and HT-only groups (43; range, 16-98), and similar health status in the RT and RT + HT groups (28; range, 12-81; and 27; range, 14-96, respectively). Most patients underwent axillary staging (799, 90.0%). The Oncotype DX RS was available for 233 patients (26.2%) with a median Oncotype DX RS of 13.0 (range, 0-39). In this selected cohort of nonchemotherapy-receiving patients, only 6 had an Oncotype DX RS >25.

Treatment

A total of 516 patients (58.1%) received adjuvant RT: 342 (66%) underwent whole-breast RT (77% of whom received hypofractionated RT), 54 (11%) received partial breast RT, and the remaining 120 (23%) received RT outside of our center, and thus had limited records to discern treatment type. Of 781 (88.0%) patients initiating HT, 631 (71.1%) completed a full course or remained adherent at last follow-up. Among all patients, 118 (13.3%) received adjuvant RT alone, 233 (26.2%) received HT alone, 398 (44.8%) received both HT and RT, and 134 (15.1%) received neither HT nor RT. Five patients did not have adequate documentation after surgery to be classified by adjuvant treatment group and were therefore excluded from the analyses. Per the study design, no patients received adjuvant chemotherapy.

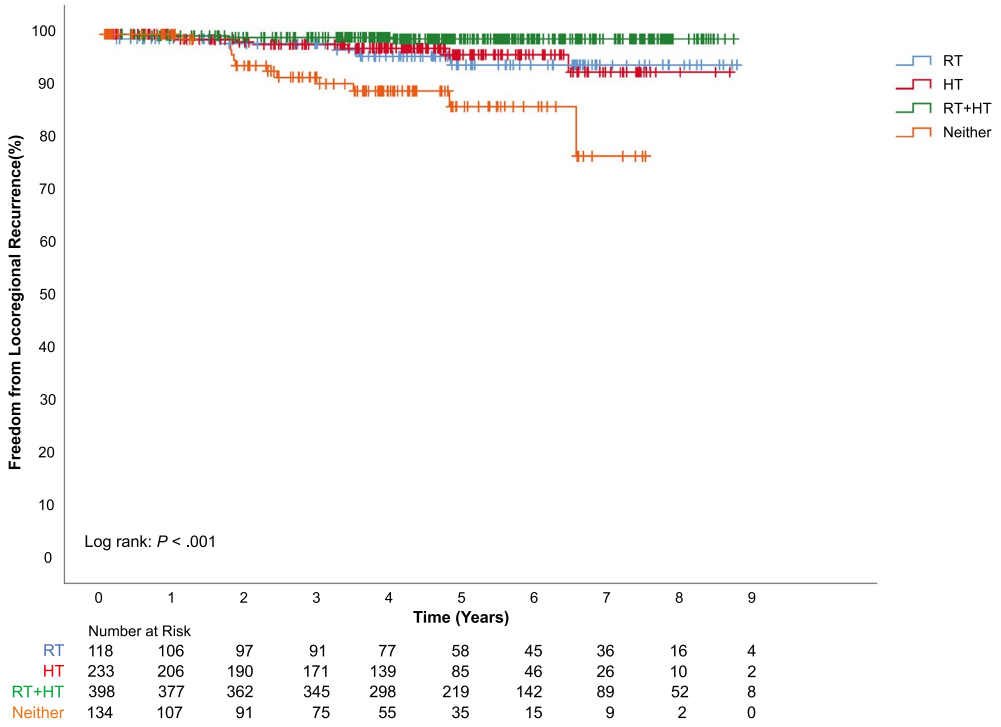
Recurrence

Overall, there were 27 LRR events, most of which were in-breast recurrences, yielding a 5-year crude LRR of 3% (Table 2). The median time to event was 2.3 years; excluding 1 local recurrence at 35 days, the range of the remaining 26 LRR events was 0.5 to 7.1 years. There was a trend toward a difference in crude LRR rates between patients who underwent sentinel lymph node biopsy versus no nodal evaluation (2.6% vs 6.7%; $P = .05$). LRR rates differed significantly by treatment received: 5-year LRR was 11% for those receiving no adjuvant treatment, 3% for HT alone, 4% for RT alone, and 1% for HT and RT (log-rank $P < .001$; Fig. 1). Cox regression analysis including all clinicopathologic variables showed that the adjuvant treatment group was the only significant predictor of LRR on backward stepwise regression. Compared to no adjuvant therapy, combination HT and RT was significantly associated with the greatest reduction in LRR (HR, 0.05; 95% CI, 0.02-0.19; $P < .001$). However, HT or RT monotherapy each yielded similar reductions in LRR: HT alone (HR, 0.27; 95% CI, 0.10-0.68; $P = .006$) and RT alone (HR, 0.32; 95% CI, 0.11-0.92; $P = .034$). Upon sensitivity analysis, excluding the single LRR event at 35 days postoperatively did not significantly change our findings.

Eleven DR events were observed, yielding a 5-year crude DR rate of 1% (Table 2). There was a marginal difference in DR rate between adjuvant treatment groups: 5-year DR rates were 3% for those receiving no adjuvant treatment, 0% for HT alone, 3% for RT alone, and 0% for HT and RT (log-rank $P = .05$; Fig. 2).

Death

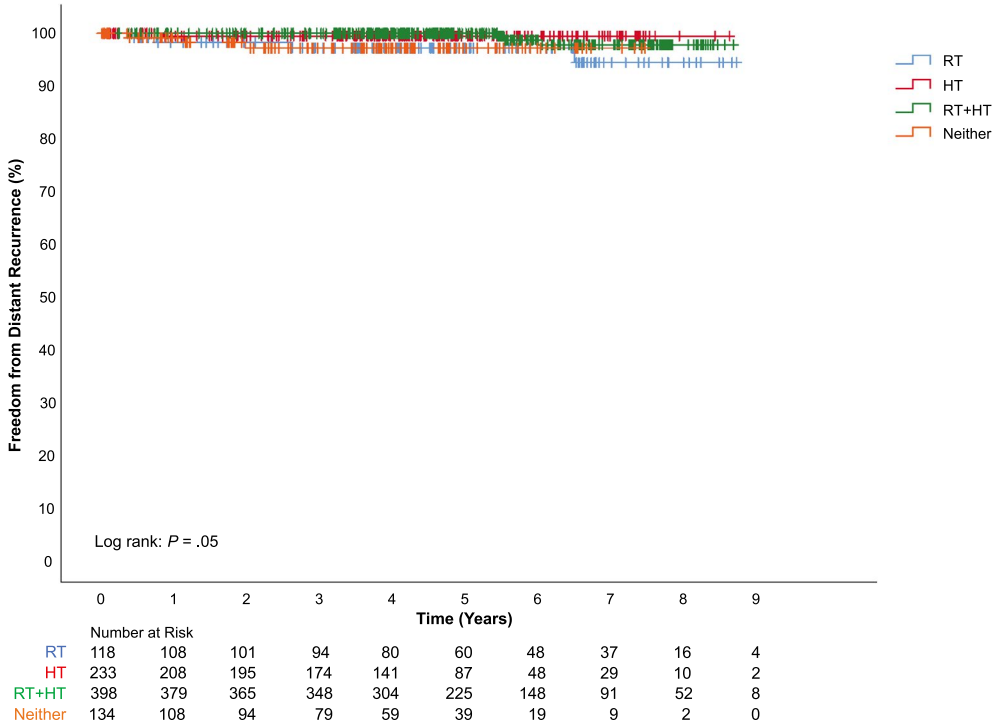
During the follow-up period, 65 (7.3%) patients died with only 3 deaths (0.1%) caused by breast cancer, yielding 5-year BCSS and OS rates of 100% and 95%, respectively, with no significant difference in BCSS between the adjuvant treatment groups. Cox regression analysis including all clinicopathological variables showed that treatment was not significantly associated with survival.



Number at Risk

RT	118	106	97	91	77	58	45	36	16	4
HT	233	206	190	171	139	85	46	26	10	2
RT+HT	398	377	362	345	298	219	142	89	52	8
Neither	134	107	91	75	55	35	15	9	2	0

Figure 1. Freedom from locoregional recurrence stratified by treatment group. HT indicates hormonal therapy; RT, radiation therapy



Number at Risk

RT	118	108	101	94	80	60	48	37	16	4
HT	233	208	195	174	141	87	48	29	10	2
RT+HT	398	379	365	348	304	225	148	91	52	8
Neither	134	108	94	79	59	39	19	9	2	0

Figure 2. Freedom from distant recurrence as stratified by treatment group. HT indicates hormonal therapy; RT, radiation therapy

DISCUSSION

Within our study cohort, we observed no discernable differences in recurrence or survival outcomes between those receiving RT, HT, or both, whereas those who received neither RT nor HT exhibited significantly worse LRR. Of the 888 women, only 3 (0.1%) died of breast cancer, whereas 62 (7.0%) died of other causes, such that treatment selection had no breast cancer–specific survival implications. Distant recurrences were rare with a cumulative incidence of 1.2% and with marginally different 5-year DR rates among groups: 3% for those receiving no adjuvant treatment, 0% for HT alone, 3% for RT alone, and 0% for HT and RT. These absolute differences were small and did not show any survival implications.

In recent decades, several landmark studies have found that LRR is significantly reduced by RT after BCS.[4-6,18,20,21] Without RT, LRR among otherwise favorable-risk patients approximates 13% to 39%, with variations attributable to differences in patient selection, length of follow-up, and differences in other adjuvant treatments.[22] Despite the benefit of RT with respect to LRR, several efforts have investigated the feasibility of omitting RT in those with lower-risk features, such as older age, wider margins, smaller tumors, node–negative, and hormone-sensitive tumors.[23-26] Most of these trials, albeit with different study designs, showed a decrease in recurrence with RT, but no significant change in disease-free survival or OS in this otherwise favorable population. Our results are consistent with others' showing that RT and/or HT yield improvements in LRR without necessarily affecting BCSS or OS among favorable cohorts. To address this important question prospectively, NRG-BR007 is a phase 3 clinical trial that seeks to assess outcomes after omission of RT in this favorable cohort of older women (age ≥70 years) with node–negative, hormone receptor–positive breast cancer with low oncotype score.[27]

Just as several trials have reported on the benefits of RT in reducing recurrence rates after BCS, other studies have addressed the use of HT in treating those with hormone-responsive tumors, albeit in younger cohorts.[9,11,28,29] In the NSABP B-21 trial, researchers compared HT and/or RT and found that tamoxifen may be less effective than RT at preventing in-breast tumor recurrence after BCS, whereas the combination of both RT and HT was more locally effective than either alone.[18] Notably, the treatment groups (RT alone, tamoxifen alone, RT + tamoxifen) did not differ significantly in terms of DR, although this study was conducted in an era that preceded routine ER testing. Our findings, among a more favorable cohort of patients with breast cancer, are consistent with the B-21 findings, recapitulating similar DR rates across groups. Our findings also parallel the results of the BASO (British Association of Surgical Oncology) II trial that evaluated younger women (age <70 years) who underwent BCS for primary invasive breast cancer (<2 cm in diameter). Using a 2 × 2 factorial design, 1135 patients were randomized to adjuvant RT ± tamoxifen, showing that LRR was reduced to a similar extent by either RT or HT monotherapy (HR, 0.37 and HR, 0.33, respectively).[30]

It is well established that HT improves BCSS and OS,[7,8] yet little data exist regarding older patients' competing mortality risks with respect to the benefit of adjuvant HT on survival outcomes. Most studies in this population have also focused on the relative benefit of adding RT to HT rather than on comparing the 2 monotherapies directly. Murphy et al reported that HT nonadherence was significantly associated with distant metastasis and disease-free survival, concluding that RT alone may be appropriate for older patients.[31] Khan et al further reported no difference in 10-year contralateral breast relapse, distant metastasis-free survival, or OS among those receiving RT with or without HT.[32] Our data similarly suggest that omitting HT in the setting of RT monotherapy does not compromise locoregional control or survival outcomes. The baseline health status of patients receiving both RT and HT in this study was comparable with those receiving RT alone, yet we still did not observe a clinically significant decrement in omitting HT in these healthier patients.

This analysis was prompted by several reports among similar populations, which showed that neither RT nor HT influence survival outcomes but with limited data to guide LRR risk prediction.[33,34] Indeed, given the exceedingly favorable risk profiles of patients in these analyses, it remains exceedingly difficult to identify survival differences based on adjuvant therapy selection. Therefore, we have highlighted locoregional outcomes in our analyses. Several studies, such as the Milan III (Milan Cancer Institute), have shown that older age portends more favorable breast cancer outcomes.[35] Moreover, with fewer remaining life-years, an older patient has a shorter time horizon during which to manifest the benefit of adjuvant therapy for an indolent malignancy that may not yield a clinically significant recurrence for many years.[36] Thus, the option to omit either years of HT or the local toxicities of RT may offer appropriately selected patients a personalized

approach that suits their goals and preferences. The toxicities of HT, such as thromboembolic events, bone density issues, and hot flashes, should be carefully considered when weighing the clinical benefits of these medications.[12,13] This side-effect profile and impact on health-related quality of life can also lead to poor adherence, resulting in only 50% to 66% of patients completing HT as intended.[37-39] In addition, partial breast irradiation (PBI) has emerged as an alternative to whole-breast RT in early-stage breast cancer,[40-42] and there now exist several accelerated regimens that make either PBI or whole-breast radiotherapy more convenient.[43] These novel RT approaches may be opportune for older patients given potential advantages such as shorter treatment times, improved toxicity profiles, and cost reduction. From a cost-effectiveness perspective, a recent analysis comparing HT alone for 5 years, accelerated PBI, and their combination, showed that both HT and RT monotherapy are appropriate options for patients aged 70 years or older with early-stage breast cancer.[36] Thus, if RT monotherapy provides sufficient and comparable clinical benefit to RT + HT, omission of HT may be a reasonable consideration. Analogous to our investigation, this hypothesis is being evaluated by the EUROPA (Exclusive Endocrine Therapy or Partial Breast Irradiation for Women Aged ≥70 Years with Luminal A-Like Early-Stage Breast Cancer) study, a phase 3 trial comparing PBI alone versus HT alone after BCS in adults aged ≥70 years with early-stage breast cancer.[44]

Adjuvant treatment was not associated with either BCSS or OS in this cohort upon adjusting for underlying comorbidities via SI. These findings are consistent with prior studies, including CALGB (Cancer and Leukemia Group B) 9343, which showed that only 3% of similarly favorable patients died of breast cancer, whereas 49% died of other causes after 12 years of follow-up.[21] Other studies have recapitulated these findings among similar cohorts.[24,45] The indolent low-risk profile of lesions treated in this study suggests that longer-term follow-up will be needed to fully evaluate the breadth of late recurrence and survival events. Indeed, whereas triple–negative and HER2-driven tumors yield most events within the first 5 years, ER+ lesions may recur over a longer time horizon.[46]

These findings must be interpreted in the context of the study design. The retrospective nature of our data is subject to potential bias and confounding. It is challenging to parse all the potential factors used in treatment decision-making, and there was likely confounding between treatment selection and overall health status given the differences in baseline comorbidities observed between the groups. We addressed this by adjusting for SI in our multivariable model, yet additional unaccounted factors (eg, psychological) may also play a role in treatment selection. In addition, although efforts were made to ascertain HT compliance, recall bias and patient misreporting may have influenced the accuracy of HT-adherence data. Although we evaluated a relatively large cohort of nearly 900 patients, longer follow-up will be necessary to elucidate the long-term survival implications of treatment selection given the relatively few BCSS events observed in this analysis.

In conclusion, this study reveals a low risk of LRR among a subset of older patients with hormone-receptor–positive, early-stage breast cancer in the setting of breast conservation. Although dual therapy with RT and HT maximally reduces the risk of LRR and DR, foregoing either RT or HT does not significantly increase recurrence risk at 5 years and has no influence on survival outcomes. Foregoing both RT and HT, however, may yield an unacceptably high risk of LRR. Further studies will elucidate whether appropriately selected patients can feasibly receive RT monotherapy rather than the current standards of HT monotherapy or a combination of RT and HT.

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CONFLICT OF INTEREST DISCLOSURES

Monica Morrow has received honoraria from Genomic Health. The other authors made no disclosures.

AUTHOR CONTRIBUTIONS

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