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Original article

The effect of post mastectomy radiation therapy on survival in breast cancer patients with N1mic disease

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ABSTRACT

Background: The role of post mastectomy radiation therapy (PMRT) in patients with N1mic breast cancer has not been well defined. A retrospective analysis was performed using the SEER database to evaluate the impact of PMRT on survival in patients with N1mic breast cancer.
Materials and methods: Women with T1-T2, N1mic, M0 breast cancer who had undergone mastectomy were analyzed. Descriptive statistics were calculated for all variables. Univariate analysis to assess for differences in survival with respect to covariates was performed using the log rank test while multivariate analysis was performed with Cox proportional hazards regression. Sub-cohort analysis with propensity score matching was used to assess differences in survival among patients undergoing PMRT vs no PMRT. Comparisons were considered statistically significant at $P < 0.05$.
Results: Among 5878 patients, 1202 (20%) underwent PMRT. On univariate analysis, PMRT was a significant predictor of CSS, but not OS. There was no difference in either OS or CSS between the PMRT vs no PMRT groups on multivariate Cox regression analysis and after propensity score matching.
Conclusions: Among patients with T1-T2, N1mic, M0 breast IDC from the SEER database, there was no difference in either OS or CSS among patients who underwent PMRT vs no PMRT. These results suggest that PMRT does not impact survival among breast cancer patients with N1mic disease. However, additional prospective studies with longer follow up are necessary for further evaluation.

1. Introduction

Breast cancer represents the most commonly diagnosed non-cutaneous malignancy and 2nd leading cause of cancer related to death in women with an estimated 268,000 new cases and 41,760 deaths in 2019 [1]. Yet, advancements in screening and treatment has reduced the mortality rate by 40% from 1989 to 2016. Radiation therapy comprises an important aspect of treatment.

Results from the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) meta-analysis among women with invasive breast cancer after mastectomy and axillary lymph node dissection (ALND) demonstrated reductions in locoregional recurrence, overall recurrence, and breast cancer mortality in women with 1–3 and ≥4 positive lymph nodes with PMRT, regardless of administration of systemic therapy [2]. However, these benefits did not extend to women with node negative disease.

It remains unknown how these results apply to patients with nodal micrometastases, as there are no prospective data to support PMRT in these patients. The increased use of sentinel lymph node biopsy (SLNB) with step sectioning and immunohistochemistry has led to an increase in the identification of small nodal tumor foci [3]. The 5th edition of the AJCC Cancer Staging Manual initially identified micrometastatic nodal lesions as no more than 2.0 mm in diameter with subsequent editions providing a lower limit on the size defining nodal micrometastases as > 0.2 mm but ≤2.0 mm, classified as pN1mi disease [4–7].

Given that the EBGTCG meta-analysis did not provide a clear distinction or sub-analysis of pN1mi patients, the role of PMRT in these patients remains unknown. Furthermore, it is likely that any patients with pN1mi disease among the 22 trials analyzed were

Abbreviations: PMRT, Post mastectomy radiation therapy.

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classified as pN0 disease, given that older trials were accruing patients prior to the current advancements in nodal evaluation, which has allowed the detection of tumor foci less than 2 mm. Retrospective analyses have suggested that PMRT among patients with pN1mi breast cancer does not improve either recurrence rates or survival [8–10]. However, these studies are limited by either small or heterogeneous patient cohorts. The largest study involved over 14,000 patients but was based on a hospital based registry and only evaluated overall survival (OS) using the National Cancer Database (NCDB) [10].

We aimed to determine if these results could be extrapolated to a more general population using the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program, which includes data on patients representative of the U.S. population and is not limited to hospital registries like the NCDB. Moreover, the SEER database also provides information on cancer specific survival (CSS), which to our knowledge, has not been reported among pN1mi breast cancer patients undergoing PMRT using a large national database. Here, we report the results of the effect of PMRT on OS and CSS among N1mic patients from the SEER database.

2. Materials and Methods

A population based search was performed using the SEER database. SEER collects and publishes cancer incidence and survival data from population registries covering 34.6% of the US population [11]. It has been validated for use in clinical research [12]. Because SEER contains publicly available, de-identified data, the National Cancer Institute does not require institutional review board approval for use of the database.

A case listing session was performed to extract all cases of invasive ductal carcinoma (IDC) of the breast diagnosed between January 1, 2004 and December 31, 2014. Histologic *International Classification of Disease (ICD) codes (ICD-0-3)* were used to extract all cases of IDC as identified by the following code: 8500/3: Infiltrating duct carcinoma, NOS. The following site specific codes were used to verify that the tumor originated in the breast: C50.0-Nipple, C50.1-Central portion of breast, C50.2-Upper-inner quadrant of breast, C50.3-Lower-inner quadrant of breast, C50.4-Upper-outer quadrant of breast, C50.5-Lower-outer quadrant of breast, C50.6-Axillary tail of breast, C50.8-Overlapping lesion of breast, and C50.9-Breast, NOS. Only patients with T1-T2, N1mic, and M0 disease were included in the final analysis.

Patients with multiple primaries and diagnosis on autopsy/death certificate were excluded from analysis. All patients underwent mastectomy and were classified by the extent of resection as follows: total (simple), radical/modified radical, and not otherwise specified (NOS). Patients with unknown radiation status, intra-operative radiation, pre-operative radiation, and radiation both before and after surgery were excluded from analysis. Those with death occurring within 1 month of PMRT were also excluded. Only patients with either no radiation or post-operative radiation were included in the final analysis. The following covariates were also extracted for analysis: age, year of diagnosis, race, marital status, insurance, tumor stage (T1 vs. T2), laterality, grade, hormone receptor status (ER, PR, and HER2), number of regional lymph nodes positive, chemotherapy, and county level attributes such as level of education and median household income.

The primary outcome measures were times in months from diagnosis to death secondary to any cause for OS and secondary to the cancer diagnosis for CSS. Descriptive statistics were calculated for all variables and compared between patients undergoing PMRT and those without using Chi-square or Fisher's exact test for categorical variables and Student's t or Wilcoxon rank sum test for continuous variables whenever appropriate. Survival curves were generated using the Kaplan Meier method. Differences in OS and CSS between patients with PMRT and those without were assessed using the log rank test. Multivariable analysis was performed with Cox proportional hazards regression models to determine the predictive performance of covariates with respect to OS and CSS. Proportional hazards (PH) assumption was tested on all covariates based on Schoenfeld residuals. For variables that violated the PH assumption ($P > 0.05$), stratified analysis by these variables were also conducted.

Sub-cohort analysis with propensity score matching of patients undergoing PMRT vs no PMRT was also conducted. All covariates listed above were used in the matching. Balance in covariates before and after matching were assessed using *t*-test or Chi-square test. Post-matching differences in covariates were also tested using paired *t*-test and McNeamar's test to account for the cohorts being matched. Since *P* values depend on sample size and may become insignificant after matching due to reduction in sample size, as recommended, standardized differences in covariates after matching were assessed and any differences >10% were considered large differences [13]; matching process was repeated until no standardized differences >10% for any covariates were observed. After successful matching, univariate Cox models were run to assess differences in survival among patients undergoing PMRT vs no PMRT. Standard errors adjusted for clustering in matching groups.

Comparisons were considered statistically significant at $P < 0.05$. All statistical analyses were performed in SPSS, version 24 (IBM Corporation) and Stata, version 14 (StataCorp LLC).

3. Results

3.1. Demographics

A total of 5878 patients met inclusion criteria. There were 1202 (20%) patients who underwent PMRT and 4676 (80%) who did not. PMRT patients were more likely to be younger, have T2 tumors, grade III disease, ER/PR/HER2 negative status, ≥4 involved lymph nodes, and to undergo chemotherapy ($P < 0.05$). The remaining demographics for the cohort after stratification by PMRT status are summarized in Table 1.

3.2. Survival analysis

On univariate analysis, there was no difference in OS with respect to PMRT. Patients undergoing PMRT demonstrated a significantly worse CSS as compared to patients not undergoing PMRT ($P = 0.007$, eFig. 1). However, no statistically significant difference in either OS or CSS was observed between the two arms on multivariate Cox regression analysis or propensity score analysis after adjustment for covariates (Table 2, eTables 1-2, Fig. 1).

On Cox regression, PMRT demonstrated similar OS to no PMRT (Hazard ratio [HR], 1.03; 95% CI, 0.84–1.25; $P = 0.794$). The following covariates were associated with significantly worse OS: older age, Black race, widowed/divorced/separated status, uninsured status, T2 stage, moderately and poorly differentiated grade, negative ER/PR/HER2 status, unknown HER2 status, and diagnosis after 2010. In contrast, involvement of <4 lymph nodes, chemotherapy, and greater baseline educational/income status were associated with improved OS. The remaining HRs, 95% CIs, and p-values are summarized in Table 2.

PMRT also demonstrated similar CSS to no PMRT on Cox regression (HR, 0.98; 95% CI, 0.77–1.25; $P = 0.862$). Additionally, the following covariates were associated with a significantly worse CSS: older age, Black race, uninsured status, T2 stage, moderately and poorly differentiated grade, negative ER/PR/HER2 status, and

Table 1
Demographics stratified by PMRT status.

	Post-Mastectomy Radiation				
	No (N = 4676)		Yes (N = 1202)		P-value
Demographics	Total	%/SD [1]/Range	Total	%/SD [1]/Range	
Age at Diagnosis					
Mean ± SD	56.8	±13.9	51.7	±13.1	<0.001
Median (min, max)	55	(19, 101)	50	(22, 92)	<0.001
Age at Diagnosis Group					<0.001
≤40	520	11%	243	20%	
41-50	1204	26%	379	32%	
51-64	1608	34%	385	32%	
≥65	1344	29%	195	16%	
Race					0.091
White	3673	79%	924	77%	
Black	482	10%	152	13%	
Asian/Pacific Islander	455	10%	114	9%	
Native American/Unknown	66	1%	12	1%	
Marital Status					0.003
Married/Partner	2807	60%	734	61%	
Single	585	13%	189	16%	
Widowed/Divorced/Separated	1091	23%	235	20%	
Unknown	193	4%	44	4%	
Insurance					<0.001
Some Medicaid	356	8%	99	8%	
Other Insurance	3018	65%	829	69%	
Uninsured	52	1%	23	2%	
Unknown	1250	27%	251	21%	
T Stage					<0.001
T1	2670	57%	487	41%	
T2	2006	43%	715	59%	
Laterality					0.014
Right	2338	50%	649	54%	
Left	2338	50%	553	46%	
Grade					<0.001
Well differentiated (I)	710	15%	113	9%	
Moderately differentiated (II)	2094	45%	498	41%	
Poorly differentiated (III)	1724	37%	569	47%	
Undifferentiated (IV)	32	1%	5	0%	
Unknown	116	2%	26	2%	
ER Status					<0.001
Positive	3721	80%	927	77%	
Negative	772	17%	261	22%	
Unknown	183	4%	14	1%	
PR Status					<0.001
Positive	3228	69%	807	67%	
Negative	1230	26%	387	32%	
Unknown	218	5%	17	1%	
HER2 Status					<0.001
Positive	408	9%	147	12%	
Negative	1629	35%	506	42%	
Unknown	2639	56%	549	46%	
No. Lymph Nodes Positive					<0.001
1-3	4545	97%	1075	89%	
≥4	131	3%	127	11%	
Year of Diagnosis					<0.001
Before 2010	2539	54%	534	44%	
2010 and After	2137	46%	668	56%	
Chemotherapy					<0.001
No	2202	47%	196	16%	
Yes	2474	53%	1006	84%	
Mastectomy					0.138
Total (Simple)	2476	53%	599	50%	
Radical/Modified Radical	2182	47%	599	50%	
NOS	19	0%	4	0%	
% w/o 9th grade education					0.003
<6%	2359	50%	669	56%	
6 - <12%	1660	36%	396	33%	
≥12%	657	14%	137	11%	
Median household income					0.408
<38K	352	8%	104	9%	
38K - <48K	615	13%	166	14%	
48K - <63K	1967	42%	508	42%	
≥63K	1742	37%	424	35%	

[1]Standard Deviation.

Table 2
Cox proportional hazard model for overall survival.

Variable	Hazard Ratio	[95% CI]	P-value
Post-Mastectomy Radiation			
No	Ref	–	–
Yes	1.03	[0.84, 1.25]	0.794
Age at Diagnosis Group			
≤40	Ref	–	–
41-50	0.89	[0.64, 1.22]	0.462
51-64	1.29	[0.96, 1.73]	0.090
≥65	3.35	[2.49, 4.50]	<0.001
Race			
White	Ref	–	–
Black	1.26	[1.03, 1.56]	0.027
Asian/Pacific Islander	0.95	[0.71, 1.26]	0.701
Native American/Unknown	1.19	[0.61, 2.32]	0.614
Marital Status			
Married/Partner	Ref	–	–
Single	1.05	[0.82, 1.34]	0.711
Widowed/Divorced/Separated	1.37	[1.16, 1.63]	<0.001
Unknown	0.84	[0.54, 1.33]	0.467
Insurance			
Some Medicaid	1.22	[0.91, 1.64]	0.178
Other insurance	Ref	–	–
Uninsured	2.22	[1.21, 4.09]	0.010
Unknown	1.07	[0.89, 1.28]	0.466
T Stage			
T1	Ref	–	–
T2	1.65	[1.42, 1.93]	<0.001
Laterality			
Right	Ref	–	–
Left	0.96	[0.83, 1.11]	0.583
Grade			
Well differentiated (I)	Ref	–	–
Moderately differentiated (II)	1.58	[1.19, 2.10]	0.002
Poorly differentiated (III)	2.05	[1.53, 2.75]	<0.001
Undifferentiated (IV)	1.67	[0.75, 3.72]	0.209
Unknown	0.98	[0.51, 1.89]	0.961
ER Status			
Positive	Ref	–	–
Negative	1.47	[1.17, 1.84]	0.001
Unknown	1.64	[0.58, 4.66]	0.353
PR Status			
Positive	Ref	–	–
Negative	1.63	[1.32, 2.00]	<0.001
Unknown	0.75	[0.27, 2.07]	0.578
HER Status			
Positive	Ref	–	–
Negative	1.91	[1.19, 3.08]	0.007
Unknown	3.00	[1.40, 6.42]	0.005
No. Lymph Nodes Positive			
1-3	0.44	[0.34, 0.56]	<0.001
≥4	Ref	–	–
Year of diagnosis			
Before 2010	Ref	–	–
2010 and After	1.93	[1.03, 3.63]	0.041
Chemotherapy			
No	Ref	–	–
Yes	0.67	[0.57, 0.80]	<0.001
Mastectomy			
Total (Simple)	Ref	–	–
Radical/Modified Radical	1.15	[0.98, 1.34]	0.084
NOS	0.83	[0.20, 3.39]	0.792
% w/o 9th grade education			
<6%	Ref	–	–
6 - <12%	0.90	[0.77, 1.06]	0.214
≥12%	0.72	[0.56, 0.92]	0.010
Median Household Income			
≤38K	Ref	–	–
38K - <48K	0.83	[0.63, 1.10]	0.198
48K - <63K	0.76	[0.60, 0.97]	0.030
≥63K	0.72	[0.56, 0.94]	0.014

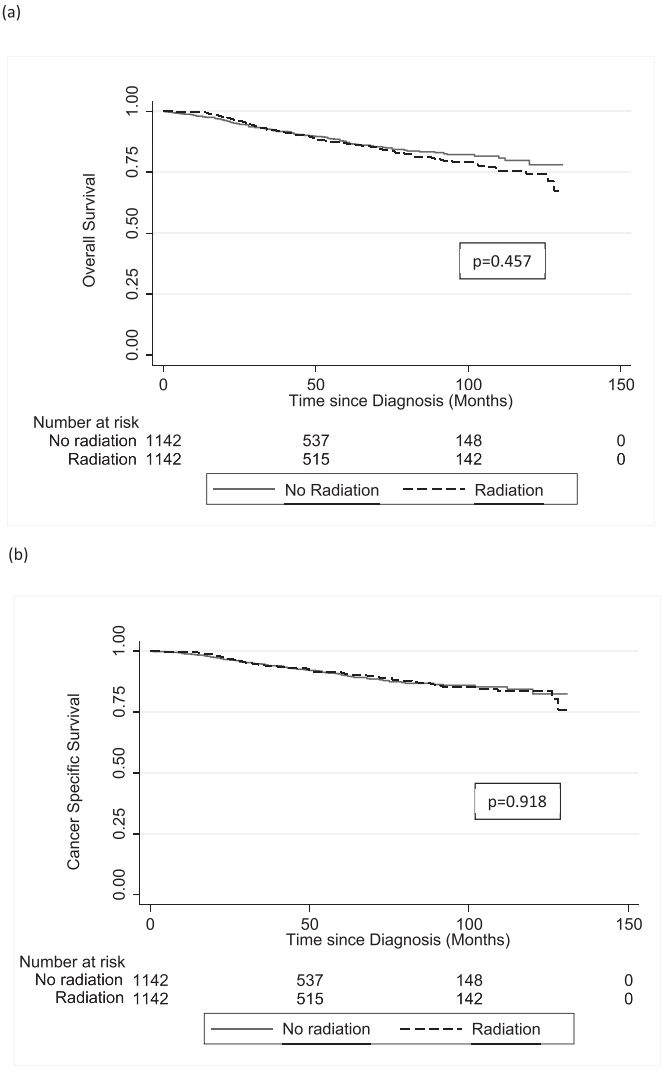

Fig. 1. Kaplan Meier curves for propensity matched data by (a) overall survival and (b) cancer specific survival.

unknown HER2 status. Involvement of <4 lymph nodes and greater baseline educational status were associated with improved CSS. Results are summarized in eTable 1.

3.3. Propensity score matched analysis

The sub-cohort of patients for propensity score matched analysis consisted of 2284 patients with 1142 patients who underwent PMRT who were matched in a 1:1 ratio to 1142 patients not undergoing PMRT. After propensity matching, there were no statistically significant differences in the distribution of covariates between the PMRT and no PMRT arms ($P > 0.05$, eTable 2). No significant differences in either OS or CSS were seen between the PMRT and no PMRT arms in the matched sub-cohorts (HR, 1.10; 95% CI, 0.87–1.38; $P = 0.436$ and HR, 0.99; 95% CI 0.74–1.31; $P = 0.918$, respectively).

4. Discussion

With the increasing prevalence of SLNB, there has been a trend towards omitting ALND among low risk breast cancer patients who may not benefit from extensive axillary management. Multiple

phase III randomized trials, including the International Breast Cancer Study Group 23–01 (IBCSG 23–01), American College of Surgeons Oncology Group Z0011 (ACSOG Z0011), and AATRM 048/13/2000 have demonstrated either non-inferiority or similar outcomes between ALND and omission of ALND in patients with limited nodal disease as identified by SLNB, including those with nodal micrometastases [14–17]. However, retrospective studies have demonstrated worse recurrence and survival rates among patients with nodal micrometastatic disease with the omission of ALND [18–20]. Additionally, there is evidence of worse outcomes among these patients when compared to node negative disease [19,21]. The discordance between phase III trials and other studies may be at least partially be explained by the use of adjuvant therapy, lack of long term follow up, and heterogeneous patient populations in terms of nodal involvement [14–16,18,19,22,23].

While randomized trials have demonstrated similar outcomes among breast cancer patients with low nodal burden with and without ALND, it is difficult to extrapolate these results to patients undergoing mastectomies. The majority of patients in IBCSG 23–01, ACSOG Z0011, and AATRM 048/13/2000 underwent breast conserving therapy (BCT) in which post-surgical radiation was standard. In IBCSG 23–01, 91% of patients underwent BCT with 97–98% of these undergoing post-surgical radiotherapy [14]. ACSOG Z001 required all patients to undergo BCT and AATRM 048/13/2000 had over 90% of patients undergoing BCT with radiotherapy [16,17]. This has led to the question of whether radiation may have led to decreased nodal recurrence rates and possibly influenced outcomes between treatment arms among these trials [22–24].

Indeed, it has been suggested that ACSOG Z0011 not be extrapolated to those patients not undergoing adjuvant radiation or only receiving partial breast irradiation in which the axillary nodes are not covered [23]. This is further supported by the results of MA.20 and EORTC 22922/10925 [25,26]. MA.20 evaluated the addition of nodal irradiation to whole breast radiation therapy (WBRT) in node positive and high risk node negative breast cancer patients. Among 1832 women, 99%, had T1-T2 tumors and 85% had between 1 and 3 positive lymph nodes. The experimental group received both WBRT and nodal irradiation to the internal mammary, supraclavicular, and axillary lymph nodes while the control group only received WBRT. With 916 patients randomized to each arm, there was an improvement in 10 year disease free survival (DFS) of 82% in the nodal irradiation arm vs 77% in the control arm, $p = 0.01$. However, no improvement in OS was noted.

Similarly, EORTC 22922/10925 demonstrated improved DFS among women with early stage, node positive or high risk, node negative breast cancer after internal mammary and supraclavicular nodal irradiation. Unlike MA.20, however, 24% of patients underwent mastectomy in the EORTC trial. In addition, there was a marginal effect on 10 year OS of 82.3% in the experimental group vs 80.7% in the control group, $p = 0.06$. A significant reduction in breast cancer mortality was also seen with nodal irradiation.

The results of these trials leads to the question of what role radiation plays in women with low nodal burden, such as those with pN1mic disease. Both MA.20 and EORTC 22922/10925 included not only node positive patients but also those with node negative disease but considered to be at high risk of nodal involvement including those with tumors $\geq$5 cm or $\geq$2 cm with <10 axillary lymph nodes dissected and with either grade III disease, ER negative hormone status, or positive lymphovascular invasion as defined on MA.20; and with central/medially located tumor as defined on EORTC 22922/10925. Thus, it is conceivable that patients with low nodal burden, i.e. pN1mi disease, may derive the same benefits as those with nonexistent nodal burden but with high risk features.

Another uncertainty involves whether the results of the aforementioned trials can be extrapolated to patients who undergo mastectomy rather than BCT as the former group is underrepresented in most trials. This is especially true among low risk post-mastectomy patients in whom radiation may be omitted altogether. Indeed, the National Comprehensive Cancer Network (NCCN) guidelines recommend omitting PMRT among patients with early stage breast cancer with negative axillary lymph nodes, tumor size $\leq$5 cm, and negative margins $\geq$1 mm [26]. Consistent with the results of the EBCTCG meta-analysis, however, PMRT is a category 2 A recommendation for patients with 1–3 positive axillary lymph nodes and a category 1 recommendation for patients with 4 or more positive lymph nodes. However, it remains unclear if patients with N1mic disease, who would be defined as low risk by NCCN otherwise, should be treated with PMRT as these patients may possibly fall in between N0 and N1 disease in terms of prognosis [27]. Thus, in order to assess this group of patients, we limited our analysis to post mastectomy patients with T1-T2 tumors (i.e. $\leq$ 5 cm in size) but with nodal micrometastases.

While analysis initially demonstrated significantly worse CSS among those undergoing PMRT, this difference was likely due to differing baseline clinical characteristics between the two treatment arms. A selection bias for PMRT was present among high risk patients as those with larger primary tumors, higher grade disease, and ER/PR/HER2 negative hormone status were more likely to undergo PMRT. These risk factors have been consistently associated with greater locoregional recurrence (LRR) and worse CSS [28–37].

In their retrospective analysis of 877 post mastectomy, node negative breast cancer patients; *Jagsi* et al. identified size >2 cm as an independent risk factor for increased LRR [38]. Indeed, patients with T2 disease, i.e. those with >2 cm disease, were more likely to receive PMRT among our cohort. Moreover, *Abdulkarim* et al. found an increased rate of LRR among patients undergoing mastectomy without PMRT as compared to those undergoing BCT with adjuvant radiation among their cohort of 768 breast cancer patients with triple negative hormonal status [37]. Again, as demonstrated among our patient cohort, PMRT was more likely among patients with a negative hormonal status. These high risk factors likely influenced patient selection for PMRT. However, after correction for baseline characteristics and high risk factors on both Cox regression and propensity score matched analysis, PMRT was no longer significantly associated with CSS.

Our results for OS are consistent with the findings of *Wu* et al. [10]. Their cohort of patients was very similar to ours, including post-mastectomy patients with pT1-2 N1mic disease. Similar to our results, no significant difference in OS was demonstrated between PMRT and no PMRT. However, they used the NCDB database. In contrast, we used the SEER database to not only study CSS, which is not collected by the NCDB, but also to determine if the results of *Wu* et al. could be extrapolated to the SEER population. One important difference between the two databases is that SEER is able to provide population based demographics and statistics whereas the NCDB data is limited to data provided by Commission on Cancer (CoC) accredited hospitals which represent only about a third of hospitals in the US. As a result, the NCDB does not contain information on many cases within pre-defined geographic locations that would be captured by SEER [39].

Multiple demographic and socioeconomic variables have been associated with cancer survival including race, marital status, insurance, education, and income [40–45]. Disparities in survival with respect to these variables include differences in social support, access to care, screening and treatment [46]. Indeed, race, marital status, insurance, and educational/income status were independent predictors of OS while race, insurance, and educational level were independent predictors of CSS among our cohort.

Limitations of this study include those inherent to retrospective analyses. Details of radiation treatment such as dose, distribution, treatment volumes, and radiation fields are not collected in the SEER database. Thus, data on the extent of PMRT including thoracic wall radiation and/or nodal irradiation is not provided. Thus, it is possible that among our cohort, a significant proportion of PMRT patients may have undergone thoracic wall irradiation without nodal irradiation and that this may have led to a lack of difference in survival between our two arms.

Finally, our analysis was limited to patients diagnosed with nodal micrometastases as defined by the 6th and later editions of the American Joint Committee on Cancer (AJCC) staging system. We limited our analysis to patients staged by the AJCC 6th and later editions as prior editions did not provide a lower size limit for nodal micrometasases. As the 6th edition was published in 2002, the earliest cases in our cohort date back to 2004. Thus, it is possible that any divergence in survival between our two arms may take additional time to emerge as early stage breast cancer has a long natural history.

It has been estimated that 1 breast cancer death is avoided within 20 years of PMRT for every 1.5 recurrences prevented within the first 10 years [2]. As these reported outcomes are based on the results of the EBCTCG meta-analysis in which the majority of patients had pN1 or greater disease, we hypothesize that if PMRT does indeed improve survival, benefits among N1mic patients may take even longer to appear as compared to patients with nodal macrometastases. This is further supported by data suggesting that patients with nodal micrometastases to have an intermediate survival rate falling in between node negative and node positive disease [27,47]. For example, in their SEER analysis of 207,720 breast cancer patients, *Chen* et al. demonstrated N1mic disease to be a significant prognostic predictor for survival with a HR of 1.35 as compared to N0 disease and 0.82 as compared to N1 disease. Both 5- and 10-year survival for pN1mic disease was intermediate between N0 and N1 nodal status [27].

Despite the limitations of this study, it is the largest retrospective analysis assessing the effect of RT on CSS in patients with N1mi breast cancer after PMRT. The strength of this study lies in the large patient population analyzed. Moreover, to our knowledge, this is the first SEER analysis assessing the role of PMRT on OS and CSS among this cohort of patients. The unique advantage of SEER over other databases is in its' tendency to capture details of the general U.S. population. Our results demonstrate similar survival outcomes between the use of PMRT and no PMRT among patients with N1mic breast IDC. However, randomized trials with longer follow up are necessary for further evaluation of the role of PMRT in this cohort of patients.

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Declaration of competing interest

The authors have no conflicts of interest to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.breast.2020.02.009.

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