

Evaluation of the 8th edition of the American joint committee on cancer's pathological staging system in prognosis assessment and treatment decision making for stage T1-2N1 breast cancer after mastectomy

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ABSTRACT

Purpose: The 8th edition of the American Joint Committee on Cancer (AJCC) pathological staging system for breast cancer considers biologic factors in addition to the anatomical features included in the previous systems. The purpose of this study was to determine the validity of the 8th AJCC staging system for T1-2N1 breast cancer and to assess the effect of additional chemotherapy and radiotherapy according to the new pathologic stages.

Methods: The cohort included patients from the Surveillance, Epidemiology, and End Results program (2010–2012) who had stage T1-2N1 invasive breast carcinoma and underwent mastectomy. All patients were restaged using the 8th AJCC staging system. The Kaplan–Meier method, Cox proportional hazards regression, and competing risks models were used for data analysis.

Results: We identified 9908 patients including 3022 (30.5%), 3131 (31.6%), 1940 (19.6%), 1194 (12.1%), and 621 (6.3%) were classified with stage IA, IB, IIA, IIB, and IIIA disease, respectively. The 5-year breast cancer-specific survival (BCSS) was 97.3%, 94.3%, 88.3%, 84.0%, and 71.1% for stage IA, IB, IIA, IIB, and IIIA disease, respectively. Higher pathological stage was associated with a significantly higher risk of breast cancer-related death. Chemotherapy was associated with better BCSS regardless of the pathological stage, but radiotherapy was only associated with better BCSS in stage IIIA disease.

Conclusions: The 8th AJCC pathological staging system provides more refined stratification for T1-2N1 breast cancer patients after mastectomy and may meet the needs of the current trend of individualized decision making for chemotherapy and radiotherapy in this patient subset.

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1. Introduction

The traditionally used American Joint Committee on Cancer (AJCC) staging system for breast cancer is based on the anatomic features including primary tumor size (T), the number and location of lymph nodes involved (N), and the distant metastasis status (M) [1]. This anatomy-based TNM breast cancer staging system has been widely used to predict prognosis and to make therapeutic

decisions worldwide. However, this system does not account for changes in molecular factors such as estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor-2 (HER2), and histological grade, which have been definitively found to have prognostic and predictive value in breast cancer evaluation and treatment [2]. Studies have indicated that the inclusion of these biological factors in the traditional anatomic staging system would be beneficial [3–8], and accordingly, some changes were made in the 8th AJCC breast cancer staging system [1,2,7,8], which is the first staging system to incorporate biological factors into the TNM staging system. The new prognostic staging system is considered to be a significantly superior tool for predicting survival outcome as compared to the previous one, and its prognostic benefits have been validated in several studies [9–15].

The traditional TNM staging system divided stage T1–2 tumors with one to three positive lymph nodes (T1–2N1) into stage IIA (T1N1) and IIB (T2N1) tumors [16]. However, in T1–2N1 breast cancers, there are significant differences in locoregional recurrence (LRR), distant metastasis (DM), and overall survival (OS) that are caused by various biological factors [17,18]. The modified staging system overcomes this issue by taking into account the high heterogeneity of stage T1–2N1 disease and classifying T1–2N1 tumors into five substages: IA, IB, IIA, IIB, and IIIA (1). This new pathological substaging seems promising, but very few studies have validated these new substages of stage T1–2N1 disease [19]. There is also some controversy about the effect of chemotherapy and post-mastectomy radiotherapy (PMRT) in patients with stage T1–2N1 disease [19–27]. To the best of our knowledge, no studies so far have tried to determine the effect of locoregional and systemic treatment in this patient subset. Given these gaps in the literature, in the present study, we have conducted a population-based assessment of the new pathological staging system for T1–2N1 breast cancers in terms of predicting survival, prognosis, and treatment effect, and investigated the effect of additional chemotherapy and PMRT on various pathologic stages in this patient subset.

2. Materials and methods

2.1. Patient selection

Patients were selected from the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute. The SEER program collects data on population-based cancer incidence, demographic and tumor characteristics, treatment, and survival for approximately 28% of the United States population [28]. Patients with stage T1–2N1 invasive breast carcinoma treated with mastectomy between 2010 and 2012 were identified from the program's database. From among them, the following patients were excluded: those who had no positive pathological diagnosis; those who were treated with non-beam external irradiation; and those for whom data on the number of lymph nodes involved, race/ethnicity, hormone receptor status, and tumor grade were unavailable. Our study was exempt from approval by the Institutional Review Board because patient data are anonymized in the SEER database.

2.2. Baseline patient characteristics

The following baseline patient characteristics were collected in our study: age, race/ethnicity, tumor grade, tumor size, histological features, the number of lymph nodes involved, ER status, PR status, HER2 status, radiotherapy, and chemotherapy. Breast cancer-specific death was defined as death caused by breast cancer. All cases were restaged using the 8th AJCC pathological staging system.

2.3. Statistical analysis

Patient characteristics between treatment arms were compared with the chi-squared test. Breast cancer-specific survival (BCSS) was evaluated using the Kaplan–Meier method and compared with the log-rank test. Cox proportional hazards regression analysis was used to assess the prognostic indicators associated with BCSS. In addition, we also used univariate and multivariable competing risk models to determine the cumulative incidence of breast cancer-related death. Competing risks models in the Cox model framework as proposed by Fine and Gray were also used to assess combined effects of the variables on breast cancer-related death. Statistical analyses were conducted using IBM SPSS 22.0 (IBM Corp., Armonk, NY) and Stata/SE version 14 (StataCorp, TX, USA). P values < 0.05 were considered to indicate statistical significance.

3. Results

3.1. Patient characteristics

Based on our study criteria, we identified 9908 patients with a median age of 57 years (range, 20–98 years). Fig. 1 depicts the patient selection flowchart in this study. Table 1 lists the patients' baseline characteristics. The majority of patients had invasive ductal carcinomas (87.0%), and were ER positive (82.5%), PR positive (72.1%), and HER2 negative (82.5%). In addition, two-thirds of the patients were above 65 years (68.5%) and Non-Hispanic White (66.7%), and had T2 stage disease (59.2%). With regard to the pathological stage, 3022 (30.5%), 3131 (31.6%), 1940 (19.6%), 1194 (12.1%), and 621 (6.3%) patients were classified as having stage IA, IB, IIA, IIB, and IIIA disease, respectively.

3.2. Correlation of treatment with patient characteristics

A total of 3482 (35.1%) patients were treated with PMRT. Younger age ($P < 0.001$), poorly differentiated/undifferentiated tumors ($P < 0.001$), larger tumor size ($P < 0.001$), a higher number of positive lymph nodes ($P < 0.001$), and treatment with chemotherapy ($P < 0.001$) were associated with a higher likelihood of treatment with PMRT. In addition, patients with higher pathological stages ($P < 0.001$) were also more likely to receive PMRT (Table 1).

With regard to chemotherapy, 66.8% ($n = 6713$) of the patients were treated with chemotherapy. Younger age ($P < 0.001$), poorly differentiated/undifferentiated tumors ($P < 0.001$), invasive ductal carcinomas ($P < 0.001$), larger tumor size ($P < 0.001$), higher number of positive lymph nodes ($P < 0.001$), absence of ER ($P < 0.001$), absence of PR ($P < 0.001$), and treatment with PMRT ($P < 0.001$) were associated with a higher likelihood of treatment with chemotherapy. In addition, patients with higher pathological stages ($P < 0.001$) were also more likely to receive chemotherapy (Table 1).

3.3. Survival and prognostic analysis

The median follow-up duration was 61 months (range, 0–83 months). A total of 1570 patients died, and breast cancer-related death occurred in 53.9% ($n = 846$) of these patients. The 5-year BCSS was 91.4%, and was 97.3%, 94.3%, 88.3%, 84.0%, and 71.1% in patients with stage IA, IB, IIA, IIB, and IIIA disease, respectively ($P < 0.001$) (Fig. 2A). Similar trends regarding the cumulative incidence estimates of breast cancer-related death were observed by prognostic stage (Fig. 2B).

According to the results of multivariate prognostic analysis, the new pathological stage was identified as an independent

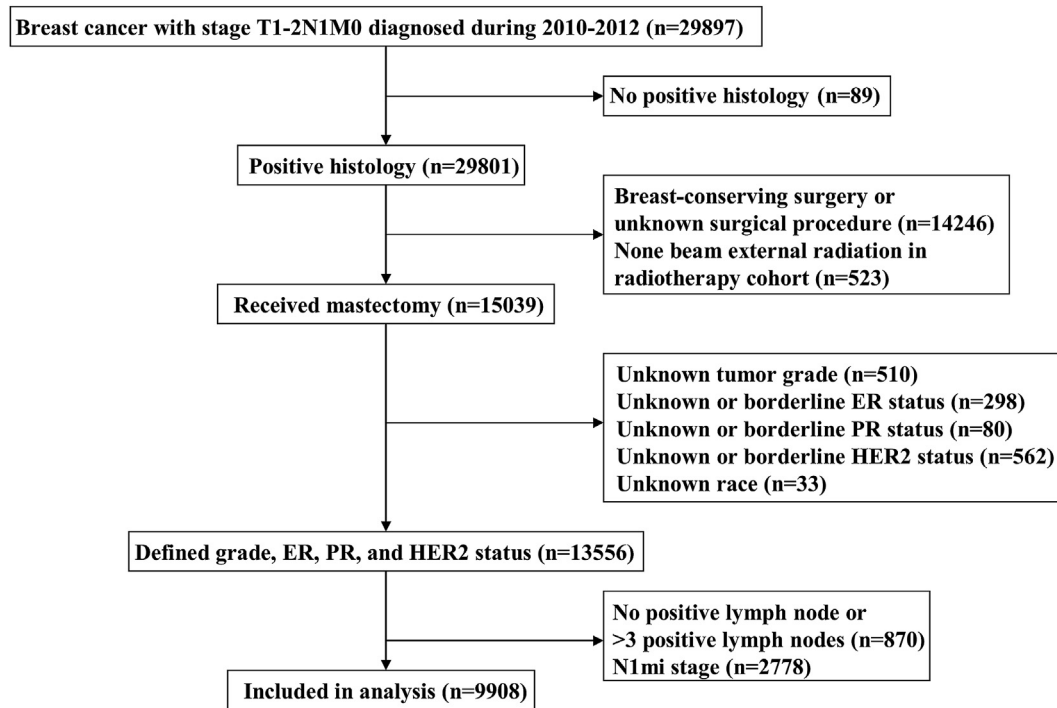


Fig. 1. The patient selection flowchart of the study.

prognostic indicator significantly associated with BCSS (Table 2). Higher pathological stage was associated with lower BCSS. The results of competing risks model in the Cox model framework also showed a higher pathological stage was associated with a higher risk of breast cancer-related death (Table 2). In addition, age, race/ethnicity, and the number of lymph nodes involved were also found to be independent prognostic factors associated with breast cancer-related death using Cox proportional hazards regression model or competing risks model.

3.4. Effect of chemotherapy and radiotherapy on BCSS according to pathological stage

We used five multivariate Cox proportional hazards models to determine the effect of chemotherapy and PMRT on BCSS according to pathological stage after adjustment for age, race/ethnicity, histological grade, and the number of lymph nodes involved (Table 3). The results indicated that treatment with chemotherapy was associated with better BCSS than treatment without chemotherapy, regardless of the pathological stage. The survival curves of patients treated with and without chemotherapy according to pathological stages are shown in Fig. 3A–F. Using competing risks models in the Cox model framework, patients treated with chemotherapy had significantly lower risk of breast cancer-related death in stage IA ($P = 0.005$), IB ($P < 0.001$), IIA ($P = 0.026$), and IIB ($P = 0.005$) disease compared to those without chemotherapy, and also had borderline effect on breast cancer-related death in stage III disease compared to those without chemotherapy ($P = 0.053$) (Table 3). The cumulative incidences of breast cancer-related death according to pathological stages are listed in Fig. 4A–F.

In the Kaplan–Meier analyses, patients treated with PMRT had better BCSS in stage IB ($P = 0.006$), IIB ($P = 0.008$), and IIIA ($P < 0.001$) disease (Fig. 5A–F). Using the multivariable Cox proportional hazards models, we only found that treatment with PMRT was associated with better BCSS than treatment without PMRT in stage IIIA disease (hazards ratio [HR] = 0.645, 95% confidence

interval [CI] = 0.460–0.905, $P = 0.011$), the 5-year BCSS was 78.9% and 65.2% in patients with and without PMRT, respectively ($P = 0.001$) (Fig. 5F). However, in patients with stage IA ($P = 0.707$), IB ($P = 0.168$), IIA ($P = 0.340$), and IIB ($P = 0.095$) disease, BCSS was comparable between those treated with and without PMRT in multivariable prognostic analysis. Similar trends were observed using univariate and multivariable competing risk models (Table 3 and Fig. 6A–F).

4. Discussion

In this study, we validated the value of the 8th edition of AJCC pathological staging system in stage T1-2N1 breast cancer after mastectomy, and further determined whether the new pathological staging system could affect the treatment decision making of chemotherapy and PMRT in this patients subset. Our results showed that the new pathological staging system could better reflect the prognosis of patients, and chemotherapy could improve BCSS in all substages, whereas PMRT could only associated with better BCSS in patients with stage IIIA disease. Our study was the first to determine the effect of the selection in locoregional and systemic treatment using the new pathological staging system.

The 8th edition AJCC pathological staging system for the first time incorporated breast cancer biologic factors into the traditionally anatomic TNM staging system. The initial model for establishing pathological staging system in the 8th edition of AJCC staging system were using 305,519 patients information from National Cancer Database between 2010 and 2012, which caused more than 35% of patients downstaged or upstaged from the 7th AJCC staging system [29]. The optimal effect for predicting prognosis in 8th AJCC staging system compared to 7th AJCC staging system has been validated in several studies [9–15]. However, limited studied focused on patients with stage T1-2N1 disease, a specific staging presented with greater heterogeneity. A study using Chinese cohort from Sun et al. ($n = 1823$) found that the 8th edition of the AJCC staging system had significant differences in LRR, DM, disease free

Table 1
Baseline characteristics of the patients included in the study cohort.

Variables	N (%)	Radiotherapy			Chemotherapy		
		No (%)	Yes (%)	P	No (%)	Yes (%)	P
Age (y)							
<65	6788 (68.5)	4065 (63.3)	2723 (78.2)	<0.001	1340 (41.9)	5448 (81.2)	<0.001
≥65	3120 (31.5)	2361 (36.7)	759 (21.8)		1855 (58.1)	1265 (18.8)	
Race/ethnicity							
Non-Hispanic White	6607 (66.7)	4344 (67.6)	2263 (65.0)	0.010	2253 (70.5)	4354 (64.9)	<0.001
Non-Hispanic Black	1107 (11.2)	672 (10.5)	435 (12.5)		298 (9.3)	809 (12.1)	
Hispanic (All Races)	1265 (12.8)	820 (12.8)	445 (12.8)		371 (11.6)	894 (13.3)	
Other	929 (9.4)	590 (9.2)	339 (9.7)		273 (8.5)	656 (9.8)	
Grade							
Well differentiated	1384 (14.0)	1021 (15.9)	363 (10.4)	<0.001	695 (21.8)	689 (10.3)	<0.001
Moderately differentiated	4524 (45.7)	2972 (46.2)	1552 (44.6)		1583 (49.5)	2941 (43.8)	
Poorly differentiated/undifferentiated	4000 (40.4)	2433 (37.9)	1567 (45.0)		917 (28.7)	3083 (45.9)	
Histological subtype							
Infiltrating ductal carcinoma	8621 (87.0)	5591 (87.0)	3030 (87.0)	0.952	2707 (84.7)	5914 (88.1)	<0.001
Lobular carcinoma	950 (9.6)	614 (9.6)	336 (9.6)		373 (11.7)	577 (8.6)	
Other	337 (3.4)	221 (3.4)	116 (3.3)		115 (3.6)	222 (3.3)	
Tumor stage							
T1	4047 (40.8)	2833 (44.1)	1214 (34.9)	<0.001	1439 (45.0)	2608 (38.8)	<0.001
T2	5861 (59.2)	3593 (55.9)	2268 (65.1)		1756 (55.0)	4105 (61.2)	
Number of positive lymph nodes							
1	5281 (53.3)	3781 (58.8)	1500 (43.1)	<0.001	1944 (60.8)	3337 (49.7)	<0.001
2	3027 (30.6)	1867 (29.1)	1160 (33.3)		871 (27.3)	2156 (32.1)	
3	1600 (16.1)	778 (12.1)	822 (23.6)		380 (11.9)	1220 (18.2)	
ER status							
Negative	1720 (82.5)	1070 (83.1)	650 (81.4)	0.011	345 (10.8)	1375 (20.5)	<0.001
Positive	8188 (17.5)	5356 (16.9)	2832 (18.6)		2850 (89.2)	5338 (79.5)	
PR status							
Negative	2760 (27.9)	1728 (26.9)	1032 (29.6)	0.004	643 (20.1)	2117 (31.5)	<0.001
Positive	7148 (72.1)	4698 (73.1)	2450 (70.4)		2552 (79.9)	4596 (68.5)	
HER2 status							
Negative	8172 (82.5)	5339 (83.1)	2883 (81.4)	0.031	2852 (89.3)	5320 (79.2)	<0.001
Positive	1736 (17.5)	1087 (16.9)	649 (18.6)		343 (10.7)	1393 (20.8)	
Pathological stage							
IA	3022 (30.5)	2173 (33.8)	849 (24.4)	<0.001	1279 (40.0)	1743 (26.0)	<0.001
IB	3131 (31.6)	1929 (30.0)	1202 (34.5)		1006 (31.5)	2125 (31.7)	
IIA	1940 (19.6)	1239 (19.3)	701 (20.1)		500 (15.6)	1440 (21.5)	
IIB	1194 (12.1)	727 (11.3)	467 (13.4)		288 (9.0)	906 (13.5)	
IIIA	621 (6.3)	358 (5.6)	263 (7.6)		122 (3.8)	499 (7.4)	
Chemotherapy							
No	3195 (32.2)	2750 (42.8)	445 (12.8)	<0.001	–	–	–
Yes	6713 (67.8)	3676 (57.2)	3037 (87.2)		–	–	
Radiotherapy							
No	–	–	–	–	2750 (86.1)	3676 (54.8)	<0.001
Yes	–	–	–		445 (13.9)	3037 (45.2)	

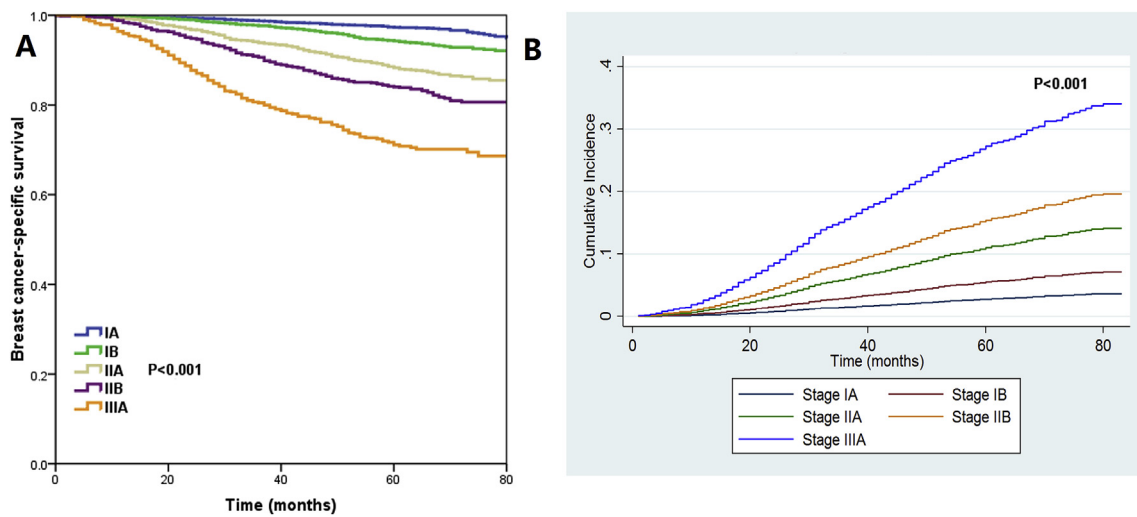


Fig. 2. Kaplan-Meier curves of breast cancer-specific survival (A) and cumulative incidence estimates of breast cancer-related death (B) stratified by prognostic stage.

Table 2
Multivariate analysis using Cox proportional hazards regression model and competing risks model to determine the prognostic indicators of breast cancer-specific survival in the patient cohort.

Variables	Cox proportional hazards regression model			Competing risks model		
	HR	95% CI	P	HR	95% CI	P
Age (y)						
<65	1			1		
≥65	1.677	1.460–1.927	<0.001	1.538	1.338–1.770	<0.001
Race/ethnicity						
Non-Hispanic White	1			1		
Non-Hispanic Black	1.122	0.925–1.362	0.243	1.126	0.923–1.374	0.243
Hispanic (All Races)	1.011	0.821–1.244	0.920	1.010	0.820–1.243	0.922
Other	0.670	0.508–0.882	0.004	0.686	0.520–0.906	0.008
Histological subtype						
Infiltrating ductal carcinoma	1			1		
Lobular carcinoma	0.990	0.758–1.292	0.938	1.010	0.773–1.320	0.936
Other	0.812	0.557–1.186	0.281	0.779	0.528–1.150	0.210
Number of positive lymph nodes						
1	1			1		
2	1.134	0.972–1.322	0.110	1.140	0.976–1.329	0.098
3	1.262	1.052–1.513	0.012	1.238	1.030–1.488	0.023
Pathological stage						
IA	1			1		
IB	2.003	1.553–2.584	<0.001	1.983	1.538–2.555	<0.001
IIA	4.149	3.241–5.310	<0.001	4.105	3.206–5.255	<0.001
IIB	5.918	4.595–7.622	<0.001	5.812	4.506–7.495	<0.001
IIIA	11.500	8.877–14.899	<0.001	11.336	8.705–14.761	<0.001

Table 3
Multivariate analysis using Cox proportional hazards regression model and competing risks model to determine the effect of chemotherapy and radiotherapy on breast cancer-specific survival according to pathological stage.

Variables	Cox proportional hazards regression model			Competing risks model		
	HR	95% CI	P	HR	95% CI	P
Stage IA						
Chemotherapy Yes vs. No	0.463	0.301–0.713	<0.001	0.552	0.332–0.820	0.005
Radiotherapy Yes vs. No	0.903	0.536–1.520	0.701	0.763	0.571–1.506	0.928
Stage IB						
Chemotherapy Yes vs. No	0.476	0.342–0.663	<0.001	0.537	0.389–0.722	<0.001
Radiotherapy Yes vs. No	0.785	0.557–1.107	0.168	0.806	0.576–1.128	0.209
Stage IIA						
Chemotherapy Yes vs. No	0.619	0.467–0.819	0.001	0.685	0.491–0.955	0.026
Radiotherapy Yes vs. No	1.152	0.861–1.543	0.340	1.162	0.869–1.559	0.315
Stage IIB						
Chemotherapy Yes vs. No	0.546	0.399–0.748	<0.001	0.621	0.446–0.865	0.005
Radiotherapy Yes vs. No	0.759	0.550–1.049	0.095	0.807	0.586–1.105	0.179
Stage IIIA						
Chemotherapy Yes vs. No	0.608	0.426–0.868	0.006	0.688	0.471–1.004	0.053
Radiotherapy Yes vs. No	0.645	0.460–0.905	0.011	0.625	0.445–0.879	0.007

survival (DFS), and OS, and it had better prognostic accuracy compared to the 7th edition of the AJCC staging system [19]. However, there were no significant difference in LRR, DM, DFS, and OS between stage IIB and IIIA disease, and there were also comparable LRR, DM, and DFS between stage IB and IIA disease [19]. The limited number of included patients was the main reason for the results by Sun et al. (IA, IB, IIA, IIB, and IIIA were 588, 530, 348, 299, and 88 patients, respectively) [19]. In our study with a larger cohort ($n = 9908$), the BCSS improved in the lower stages and worsened as the stage increased. Our study suggested that the 8th pathological staging system would be the most accurate predictor of risk stratification in patients with stage T1-2N1 disease. The new AJCC staging system better reflects the heterogeneity of stage T1-2N1 breast cancer and helps guide more detailed individualized treatment and prognosis assessment in the current clinical practice.

We noted that the patients with stage IIIA disease (T2N1, histological grade III, ER-, PR-, HER2-) showed the worst BCSS compared with other substages, with a 5-year BCSS rate of 71.1%, which suggested that triple negative breast carcinoma should be

regarded as an upstaging biologic factor [5]. Although only 6.3% of patients were in stage IIIA disease, the risk of breast cancer related death in stage IIIA disease was about seven times and double time compared to patients in stage I and II diseases, respectively. While anatomic TNM staging provides a more straightforward and easily applied system for classification of breast cancer, the newly developed pathological staging system emphasized the equality of tumor burden and tumor biologic factors in the era of personalized treatment of breast cancer [30]. This finding indicates that systemic and locoregional treatment might be changed in several anatomic stage groups. Our study supported by the recommendation from the updated guidelines by American Society of Clinical Oncology which showed that the recommendation of PMRT in stage T1-2N1 breast cancer should be based on an assessment of the individual recurrence risk using tumor and biologic characteristics [31].

As generally, stage T1-2N1 breast cancer is considered to have an intermediate risk of locoregional and distant recurrence, with much controversy regarding the adjuvant treatment. The incorporation of biologic factors into the pathological prognostic staging

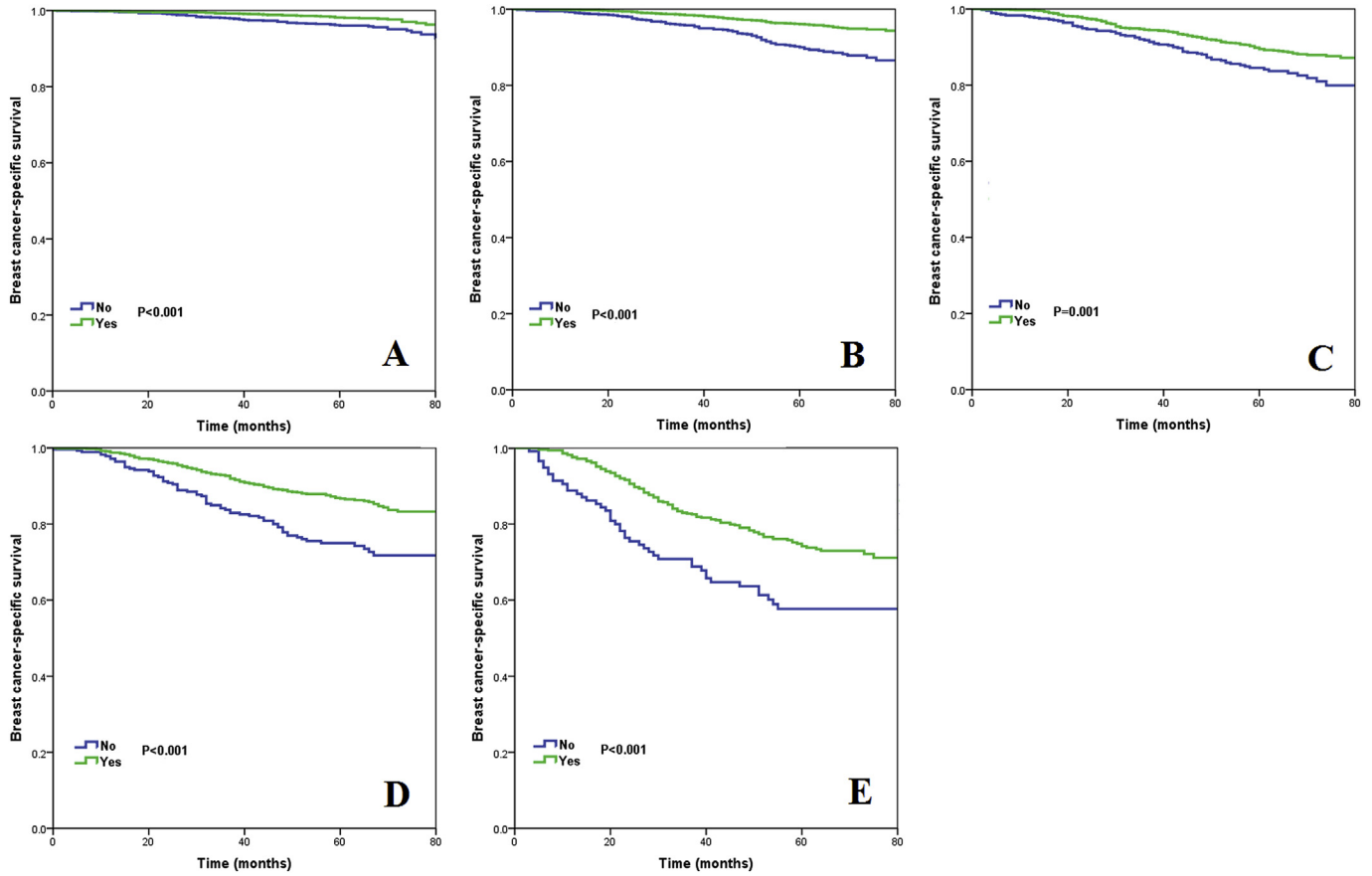


Fig. 3. Kaplan-Meier curves for assessment of the effect of chemotherapy on breast cancer-specific survival stratified by prognostic stage (A, stage IA; B, stage IB; C, stage IIA; D, stage IIB; E, stage IIIA).

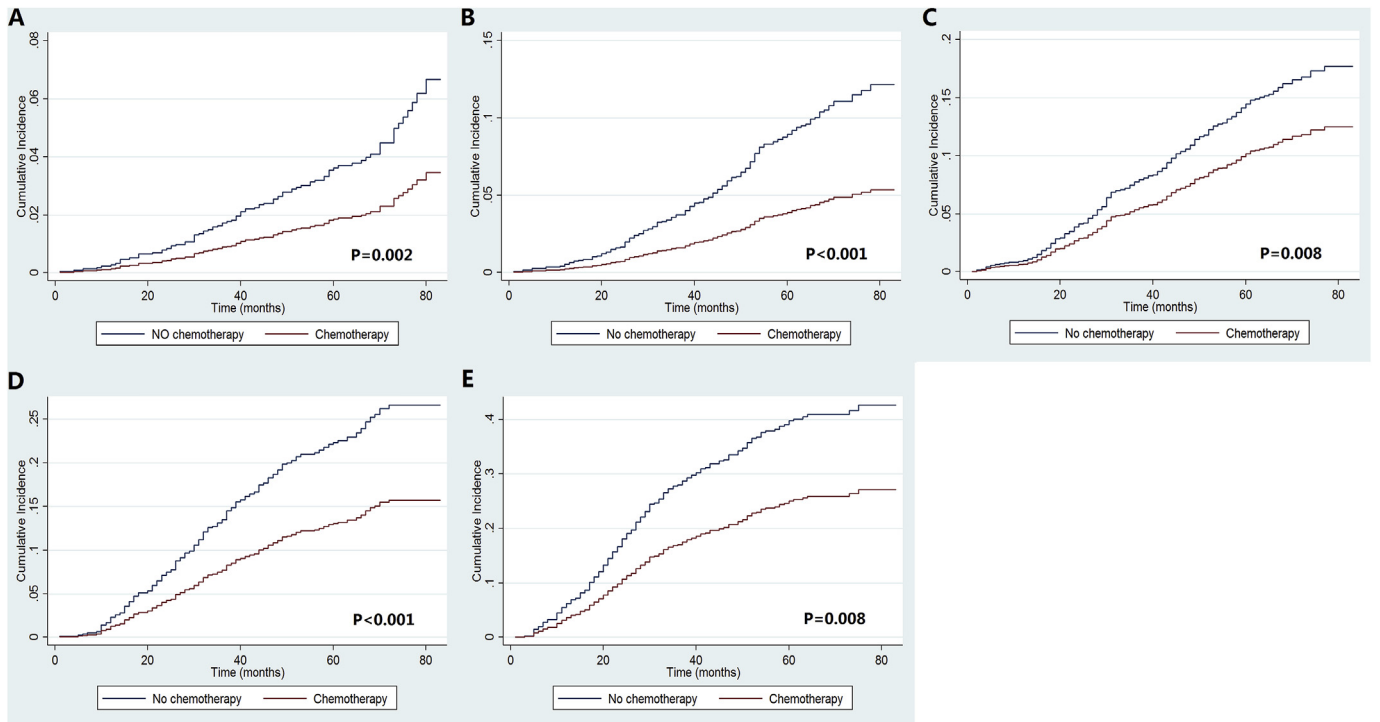


Fig. 4. Cumulative incidence estimates of the effect of chemotherapy on breast cancer-related death stratified by prognostic stage (A, stage IA; B, stage IB; C, stage IIA; D, stage IIB; E, stage IIIA).

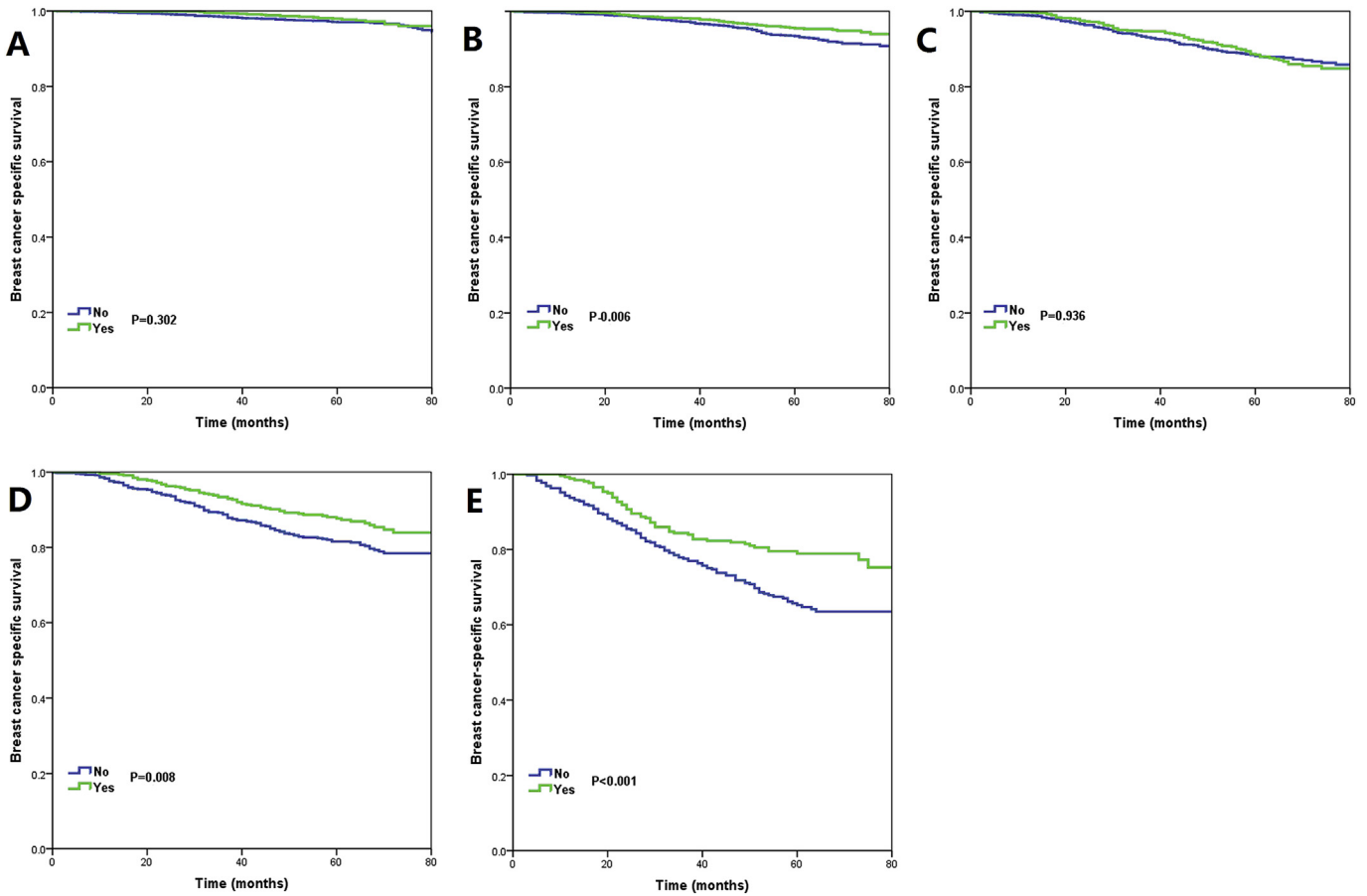


Fig. 5. Kaplan-Meier curves for assessment of the effect of radiotherapy on breast cancer-specific survival stratified by prognostic stage (A, stage IA; B, stage IB; C, stage IIA; D, stage IIB; E, stage IIIA).

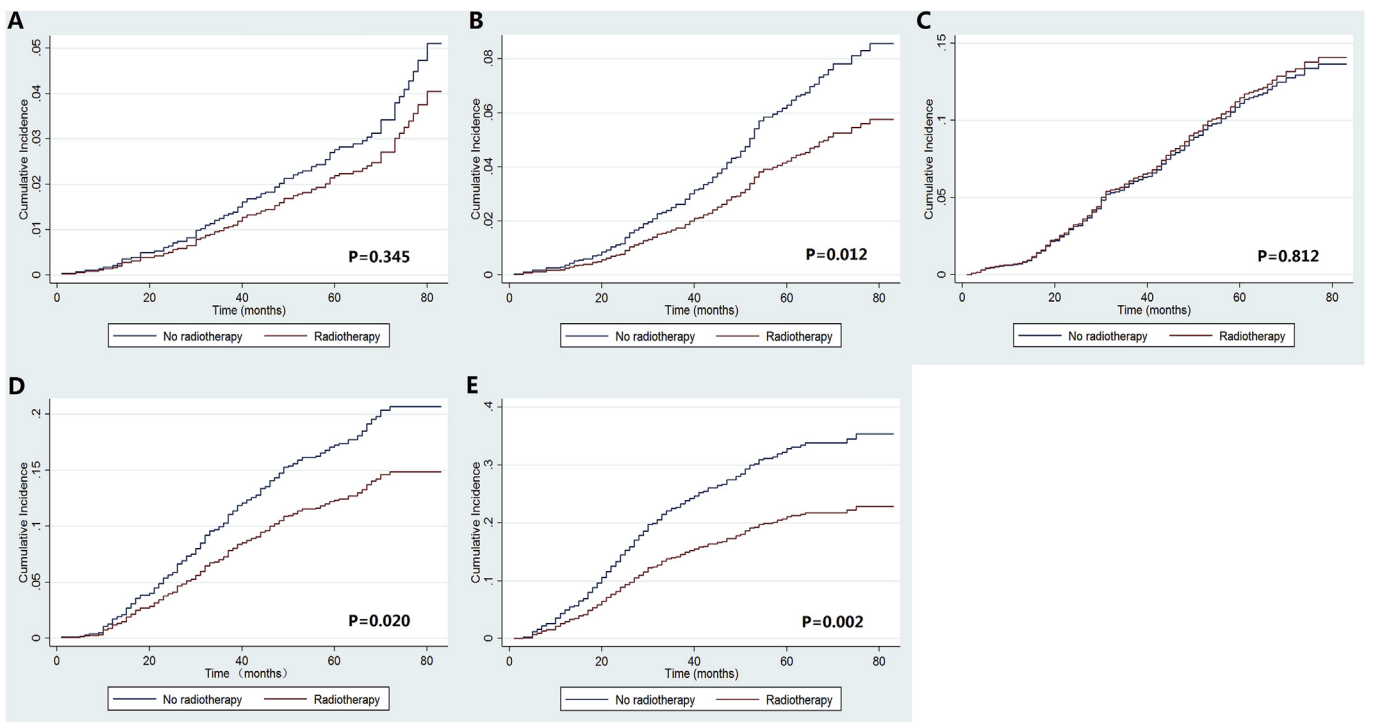


Fig. 6. Cumulative incidence estimates of the effect of radiotherapy on breast cancer-related death stratified by prognostic stage (A, stage IA; B, stage IB; C, stage IIA; D, stage IIB; E, stage IIIA).

system could better guide personalized care under more accurate prognosis prediction. However, the adjuvant treatment of breast cancer including chemotherapy and PMRT remains mainly based on the tumor size and regional nodal status in the current National Comprehensive Cancer Network (NCCN) guidelines [32]. However, the anatomic staging system might not be enough for predicting prognosis in treatment decision making [6,33]. To the best of our knowledge, there is currently no study to determine the effect of adjuvant treatment based on newly staging system. The administration of chemotherapy was significantly improved BCSS regardless of prognostic stages in our study. Although the treatment guideline from European Society for Medical Oncology does not recommend adjuvant chemotherapy for T1-2N1 patients with luminal-A subtype [34]. The guidelines from the NCCN recommend adjuvant chemotherapy for patients with lymph nodes involvement [32]. It should be noted that the new staging system is better able to determine the survival outcome of patients, and the prognosis reflected the standardized treatment based on the patient tumor and biologic characteristics [29,35]. Patients with lower stage does not mean that the patients need de-escalation of primary treatment, but rather reflects that the patient has better biological characteristics or more effective response to treatment.

The effect of PMRT in stage T1-2N1 breast cancer is vigorously debated. Although the meta-analysis from Early Breast Cancer Trialists' Collaborative Group provides a high-level evidence to guide decision-making of PMRT [36]. A higher rate of LRR in the non-PMRT in above meta-analysis [36], stage migration with sentinel node biopsy, and possible adverse events of PMRT may influence the decision-making of PMRT in this patient subset [25]. The secondary analyses of two prospective studies have indicated the administration of PMRT was related to better locoregional control (10-years LRR 2–2.5% vs. 6.5–9.0%). However, there were comparable survival outcomes between the treatment arms [23,24]. Therefore, in the modern era of individualized treatment, most stage T1-2N1 patients may not need additional PMRT [26]. However, there were no decisive tools to predict the benefit of PMRT in this patient subset in the current clinical practice.

Due to the limitation of the SEER database, we were unable to obtain the data of LRR. According to the data form 1823 patients (17.2% of patients treated with PMRT) by Sun et al., the 5-year LRR was less than 5% in stage IA and IB diseases, approximately 7%, 12%, and 16% in patients with stage IIA, IIB, and IIIA disease, respectively [19]. However, they were not analysis the effect of PMRT by different pathological stages. In this study, we further assessed whether the new AJCC staging system could guide the optimal administration of PMRT. Our study found that PMRT could only improve BCSS in patients with stage IIIA, while PMRT was not associated with better BCSS in stage IA, IB, IIA, and IIB disease compared to those without PMRT. Our study indicated that the pathological prognostic stage system incorporated the anatomic tumor burden and tumor biologic factors might provide accurate predictor of effect of PMRT in stage T1-2N1 breast cancer.

Several limitations in the present study should be acknowledged. First, the intrinsic bias in retrospective designs should not be neglected. Second, the data of chemotherapy and radiotherapy receipt are known to be under-reported in the SEER program. Third, the information on anti-Her2 treatment and hormone therapy was also not recorded in the SEER database, which might impact the prognostic assessment. Moreover, the sequencing of chemotherapy and radiotherapy, information on locoregional and distant recurrence were not collect in the SEER database. However, the primary strength of our study was the first to determine the effect of additional systemic therapy and PMRT in various new pathologic stages in stage T1-2N1 breast cancer after mastectomy.

In conclusion, the 8th AJCC prognostic staging system has the

advantage of providing more refined stratification of T1-2N1 breast cancer after mastectomy, and meets the needs of the current trend of individualized decision making with regard to chemotherapy and radiotherapy in this patient subset. Future prospective studies must be conducted in different populations to validate our results.

Declaration of competing interest

The authors have no conflicts of interest to disclose.

Acknowledgments

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