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Postmastectomy radiation therapy for patients with pT1–2N1 breast cancer over 2 decades in Korea: Korean Radiation Oncology Group 14–21

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Purpose: This study investigates patterns of postmastectomy radiation therapy (PMRT) use in patients with pT1–2N1 breast cancer treated with mastectomy in Korea over 2 decades.

Materials and Methods: Data from 700 patients treated at 16 institutions across three decades (1990, 2000, and 2010) were retrospectively reviewed.

Results: Overall, 10.0% of patients received PMRT, with utilization rates of 7.4%, 8.8%, and 11.1% in 1990, 2000, and 2010, respectively. The use of PMRT varied substantially among the hospitals (0%–87.5%). The two-dimensional radiotherapy was used in 1990, but the adoption of tangential beam three-dimensional conformal radiotherapy increased in subsequent decades. Axillary irradiation was performed in all patients in 1990 but was omitted in some cases starting in the 2000s (performed in 72.7% of cases in 2000, 84.1% in 2010). The inclusion of axillary levels, internal mammary nodes, and supraclavicular nodes decreased over time. The 10-year overall survival (OS) and recurrence-free survival (RFS) rates for all patients were 81.3% and 76.3%, respectively. Locoregional recurrence rates were significantly lower in the PMRT group (1.4%) compared to the no-PMRT group (8.1%, p=0.043). However, no significant differences were observed in 10-year OS, RFS, or distant metastasis–free survival rates between the two groups.

Conclusion: PMRT was performed in approximately 10% of patients with pT1–2N1 breast cancer after mastectomy, with minimal changes in utilization rates over two decades. The use and extent of regional nodal irradiation has declined over time. Further research is needed to reflect the latest patterns of practice.

Keywords: Breast neoplasms, Physicians' practice patterns, Radiotherapy, Mastectomy

Introduction

Postmastectomy radiotherapy (PMRT) plays an important role in the management of locoregionally advanced breast cancer. Multiple clinical trials have shown treatment benefits of PMRT in locoregional control, disease-free survival, and overall survival (OS) in patients with four or more positive axillary lymph nodes (LN) (N2 or higher) or T3–4 disease [1,2]. Despite the publication of the American Society of Clinical Oncology (ASCO) guideline and other similar guidelines over two decades ago, the benefit of PMRT in patients with a tumor size of 5 cm or smaller and metastasis to 1–3 axillary LN(s) (T1–2N1) remains unclear [3-6]. It is very challenging to determine the usefulness of PMRT since no randomized study has been conducted to assess the therapeutic value of PMRT for T1–2N1 breast cancer patients, and the patient characteristics between the PMRT and no-PMRT groups were not comparable in the retrospective studies. Most guidelines and consensus statements published in the 2000s indicate that there is insufficient evidence to support the routine use of PMRT for treating T1–2N1 disease and recommend its use exclusively for patients with poor prognostic factors [7-9]. Therefore, in the previously published studies, PMRT was performed according to each physician's preference and institutional policy [10-13]. In Korea, there is no consensus of PMRT for T1–2N1 breast cancer. Nationwide surveys conducted by the Korean Radiation Oncology Group (KROG) have shown considerable variations in patterns of PMRT [14,15].

This study was to investigate practice patterns of PMRT for T1–2N1 breast cancer and longitudinal changes over 2 decades (1990, 2000, and 2010) in Korea, enabling us to establish the future treatment guidelines for T1–2N1 breast cancer.

Materials and Methods

1. Patients

The KROG authorized this study protocol (protocol No. KROG 14-21). Using three independent patient cohorts from the years of 1990, 2000, and 2010, we collected the data of T1–2N1 breast cancer patients who were treated with mastectomy at 15 institutions in Korea. The institutional review board of each institution approved this study. Patients who were pathologically diagnosed with T1–2N1 stage breast cancer were considered eligible for this study. Patients were excluded from the study if they met the following criteria: (1) had received neoadjuvant chemotherapy, (2) had a past history of other cancers except for thyroid/skin/uterine cervix cancer and distant metastasis, or (3) were male. Finally, a total of 700 selected patients were reviewed retrospectively.

2. Data collection

Patients' data related to the following pathologic features were obtained: pathological type, nuclear grade, histological grade, tumor size, resection margin, lympho-vascular invasion, status of hormone receptors, HER2/neu status, Ki-67 expression, number and size of positive axillary LN, and extracapsular extension of axillary LN, the recurrence pattern, and the date and cause of death. Treatment information including surgical technique used for axillary LN, radiotherapy (RT), adjuvant chemotherapy, and hormonal therapy was carefully reviewed.

3. Statistical analysis

The medians and distributions were compared using the chi-square and Student's t-tests. The OS and recurrence-free survival (RFS) were estimated using the Kaplan-Meier method. Multivariate logistic regression analyses were used to assess the correlation between the variables and survival. A p-value <0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 25 (IBM Corp., Armonk, NY, USA).

Results

1. Patients' characteristics

The patients and their tumor characteristics stratified by the study year are presented in Table 1. The numbers of patients receiving mastectomy in the years 1990, 2000, and 2010 were 54, 251, and 395, respectively. The median age was 48 (interquartile range [IQR], 42 to 56) of all patients. In 1990, the proportions of premenopausal and postmenopausal patients were similar, whereas the proportion of premenopausal patients increased in 2000 and 2010. The proportion of patients with more advanced features, such as T2 disease, three positive LNs, or LN size of ≥ 10 mm, significantly decreased in recent years. While the molecular subtypes in 2000 and 2010 were comparable, 1990 showed a notable difference due to a higher proportion of cases categorized as not available.

Axillary LN dissection was performed in all patients. Sentinel lymph node biopsy (SLNB) was not adopted in the 1990 patient cohort. SLNB was conducted in 6.3% and 73.1% of the patients from the 2000 and 2010 cohorts, respectively. Number of dissected LNs has decreased over time. Adjuvant chemotherapy was given to 83.3%, 95.6%, and 91.9% of patients in 1990, 2000, and 2010, respectively. Majority of the patients (95.6%) received CMF (cyclophosphamide, methotrexate, and 5-fluorouracil) in 1990; however, the use of CMF reduced significantly thereafter. Anthracycline-based chemotherapy was performed in 38.8% and 93.4% of the patients in 2000 and 2010, respectively. Use of hormone therapy increased over the study years. The test for HER2/neu status was

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Table 1. Patients and tumor characteristics

	Year				p-value
	Total (n = 700)	1990 (n = 54)	2000 (n = 251)	2010 (n = 395)	
No. of patients					
Age (year)					0.132
Median (range)	48 (25-84)				
< 40	126 (18.0)	11 (20.4)	54 (21.5)	61 (15.4)	
≥ 40	574 (82.0)	43 (79.6)	197 (78.5)	334 (84.6)	
Menopause (n = 689)					< 0.001
Premenopause	418 (60.7)	26 (54.2)	169 (67.9)	223 (56.9)	
Postmenopause	271 (39.3)	22 (45.8)	80 (32.1)	169 (43.1)	
Pathology					0.321
IDC	656 (93.7)	53 (98.1)	236 (94.0)	367 (92.9)	
Others	44 (6.3)	1 (1.9)	15 (6.0)	28 (7.1)	
T category					< 0.001
T1	277 (39.6)	13 (24.1)	84 (33.5)	180 (45.6)	
T2	423 (60.4)	41 (75.9)	167 (66.5)	215 (54.4)	
No. of positive nodes					0.031
1	378 (54.0)	28 (51.9)	127 (50.6)	223 (56.5)	
2	213 (30.4)	12 (22.2)	77 (30.7)	124 (31.4)	
3	109 (15.6)	14 (25.9)	47 (18.7)	48 (12.2)	
Node size (mm) (n = 330)					< 0.001
< 10	243 (73.6)	-	3 (15.0)	240 (77.4)	
≥ 10	87 (26.4)	-	17 (85.0)	70 (22.6)	
Ki-67 (%)					< 0.001
< 30	155 (22.1)	1 (1.9)	8 (3.2)	146 (37.0)	
≥ 30	79 (11.3)	0 (0)	10 (4.0)	69 (17.5)	
NA	466 (66.6)	53 (98.1)	233 (92.8)	180 (45.5)	
HER2/neu					< 0.001
(+)	175 (25.0)	0 (0)	64 (25.5)	111 (28.1)	
(–)	382 (54.6)	1 (1.9)	125 (49.8)	256 (64.8)	
NA	143 (20.4)	53 (98.1)	62 (24.7)	28 (7.1)	
Molecular subtype					< 0.001
Luminal	492 (70.3)	9 (16.7)	172 (68.5)	311 (78.7)	
HER2/neu	63 (9.0)	0 (0)	18 (7.2)	45 (11.4)	
TNBC	56 (8.0)	0 (0)	26 (10.4)	30 (7.6)	
NA	89 (12.7)	45 (83.3)	35 (13.9)	9 (2.3)	
Postmastectomy radiotherapy					0.497
Yes	70 (10.0)	4 (7.4)	22 (8.8)	44 (11.1)	
No	630 (90.0)	50 (92.6)	229 (91.2)	351 (88.9)	
Surgical methods for axillary LN					< 0.001
ALND	393 (56.1)	54 (100.0)	236 (94.0)	103 (26.1)	
SLNB ± ALND	307 (43.9)	0 (0)	15 (6.0)	292 (73.9)	
No. of dissected nodes					0.002
< 10	98 (14.0)	3 (5.6)	24 (9.6)	71 (18.0)	
≥ 10	602 (86.0)	51 (94.4)	227 (90.4)	324 (82.0)	
Adjuvant chemotherapy (n = 648)					
CMF	181 (27.9)	43 (95.6)	129 (53.75)	9 (2.5)	
Anthracycline-based	433 (66.8)	1 (2.2)	93 (38.75)	339 (93.4)	
Others	34 (5.3)	1 (2.2)	18 (7.5)	15 (4.1)	
Hormone therapy (n = 492 with hormone receptor–positive)					0.012
Yes	472 (95.9)	7 (77.8)	163 (94.8)	302 (97.1)	
No	18 (3.7)	2 (22.2)	9 (5.2)	7 (2.3)	
NA	2 (0.4)	0 (0)	0 (0)	2 (0.6)	
Trastuzumab (n = 175 with HER2/neu (+))					< 0.001
Yes	78 (44.6)	0 (0)	0 (0)	78 (70.3)	
No	97 (55.4)	0 (0)	64 (100)	33 (29.7)	

IDC, intraductal carcinoma; NA, not available; HER2, human epidermal growth factor receptor 2; TNBC, triple-negative breast cancer; LN, lymph node; ALND, axillary lymph node dissection; SLNB, sentinel lymph node biopsy; CMF, cyclophosphamide, methotrexate, and fluorouracil.

performed in only one patient from the patient cohort of 1990; however, its trend increased significantly during the subsequent study years. Seventy-eight of 175 patients (44.6%) with a positive HER2/neu status received treatment with trastuzumab.

2. Postmastectomy radiotherapy

The utilization of PMRT showed a slight increase over time. Of 700 patients, 70 patients (10.0%) received PMRT, which included 7.4%, 8.8%, and 11.1% of the patients from 1990, 2000, and 2010, respectively. However, this increase was not statistically significant. The use of PMRT varied substantially among the hospitals, ranging from 0%–87.5%. Three of the 16 institutions did not perform PMRT throughout the entire study period. Patients from these three institutions exhibit various risk factors including close resection margin, positive LN size of ≥ 2 cm, and high histologic grade, among others.

There were significant differences observed between the PMRT and no-PMRT subgroups. Patients who received PMRT were more likely to exhibit high-risk features such as three positive LNs ($p = 0.015$), positive LN size of ≥ 10 mm ($p = 0.002$), positive or close resection margin ($p = 0.006$), high grade ($p = 0.036$), extensive intraductal component ($p = 0.005$), and high levels of Ki-67 expression ($p = 0.009$) (Table 2).

RT technique stratified by the study year is listed in Table 3. For chest wall irradiation, the reverse hockey stick technique was exclusively used in 1990, but the adoption of tangential beam three-dimensional conformal RT increased in subsequent decades. Chest wall boost was performed in about 28% of the patients in the years 2000 and 2010, and the median boost dose was 9 Gy (range, 8 to 10.8 Gy). While axillary irradiation was administered to all patients in 1990, its use became selective in subsequent years, with 72.7% of patients receiving it in 2000 and 84.1% in 2010. Approximately one-quarter of the patients received a posterior axillary boost, which remained consistent throughout the study periods. The inclusion of axillary LN levels, internal mammary nodes, and supraclavicular nodes decreased over time. The most common radiation dose used was 50.4 Gy (range, 45 to 60 Gy), with a daily dose of 1.8 Gy. Hypofractionated radiation scheme (45 Gy in 15 fractions) was performed for only one patient in 2010.

3. Treatment outcomes

The median follow-up was 58.5 months (IQR, 52.3 to 121.2). The median follow-up for the 1990, 2000, and 2010 cohorts was 96.4 months (IQR, 60.8 to 161.6), 137.5 months (IQR, 83.7 to 151.1), and 54.4 months (IQR, 50.2 to 58.2), respectively. The 10-year OS, RFS, locoregional recurrence–free survival (LRRFS), and distant metastasis–free survival (DMFS) were 81.3%, 76.3%, 89.7%, and

Table 2. Patients and tumor characteristics in patients with or without PMRT

	Total	PMRT	No PMRT	p-value
No. of patients	700	70 (10.0)	630 (90.0)	
Age (year)				0.600
< 40	126	11 (15.7)	115 (18.3)	
≥ 40	574	59 (84.3)	515 (81.7)	
Pathology				0.406
IDC	656	64 (91.4)	592 (94.0)	
Others	44	6 (8.6)	38 (6.0)	
T category				0.487
T1	277	25 (35.7)	252 (40.0)	
T2	423	45 (64.3)	378 (60.0)	
No. of positive node				0.015
1	378	27 (38.6)	351 (55.7)	
2	213	26 (37.1)	187 (29.7)	
3	109	17 (24.3)	92 (14.6)	
Node size (mm) (n = 300)				0.002
< 10	243	15 (50.0)	228 (76.0)	
≥ 10	87	15 (50.0)	72 (24.0)	
Resection margin				0.006
(+)	3	2 (2.9)	1 (0.1)	
Close	90	11 (15.7)	79 (12.5)	
(–)	596	57 (81.4)	540 (85.7)	
NA	10	0 (0.0)	10 (1.6)	
Histologic grade				0.036
I	69	3 (4.3)	66 (10.5)	
II	338	27 (38.6)	311 (49.4)	
III	197	28 (40.0)	169 (26.8)	
NA	96	12 (17.1)	84 (13.3)	
Nuclear grade				0.265
I	44	3 (4.3)	41 (6.5)	
II	283	23 (32.9)	260 (41.3)	
III	187	25 (35.7)	162 (25.7)	
NA	186	19 (27.1)	167 (26.5)	
Extracapsular extension				0.290
(+)	102	10 (14.3)	92 (14.6)	
(–)	365	31 (44.3)	334 (53.0)	
NA	233	29 (41.4)	204 (32.4)	
Extensive intraductal component				0.005
(+)	187	14 (20.0)	173 (27.5)	
(–)	351	29 (41.4)	322 (51.1)	
NA	162	27 (38.6)	135 (21.4)	
Lymphovascular invasion				0.289
(+)	222	22 (31.4)	200 (31.7)	
(–)	342	39 (55.7)	303 (48.1)	
NA	136	9 (12.9)	127 (20.2)	
Ki-67 (%)				0.009
≥ 30	79	14 (20.0)	65 (10.3)	
< 30	155	20 (28.6)	135 (21.4)	
NA	466	36 (51.4)	430 (68.3)	
Molecular subtype				0.050
Luminal	492	47 (67.1)	445 (70.6)	
HER2/neu	63	3 (4.3)	60 (9.5)	
TNBC	56	11 (15.7)	45 (7.1)	
NA	89	9 (12.9)	80 (12.7)	

Values are presented as number (%).
PMRT, postmastectomy radiation therapy; IDC, intraductal carcinoma; NA, not assessable; HER2, human epidermal growth factor receptor 2; TNBC, triple-negative breast cancer.

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Table 3. Postmastectomy radiotherapy

	Total	Year			p-value
		1990	2000	2010	
No. of patients received PMRT	70 (10.6)	4 (9.5)	22 (8.8)	44 (11.8)	0.497
Chest wall RT field					0.318
RH	35 (50.0)	4 (100)	11 (50.0)	20 (45.5)	
Tangential	35 (50.0)	0 (0)	11 (50.0)	24 (54.5)	
Chest wall boost					0.420
Yes	19 (26.1)	0 (0)	7 (31.8)	12 (27.3)	
No	51 (73.9)	4 (100)	15 (68.2)	32 (72.7)	
Axillary node irradiation					0.330
Yes	57 (81.4)	4 (100)	16 (72.7)	37 (84.1)	
No	13 (18.6)	0 (0)	6 (27.3)	7 (15.9)	
Irradiated axillary node level[a)]					0.082
1	19 (33.4)	1 (25.0)	3 (18.8)	15 (40.5)	
2	10 (17.5)	0 (0)	0 (0)	10 (27.0)	
3	28 (49.1)	3 (75.0)	13 (81.2)	12 (32.5)	
Posterior axillary boost					0.979
Yes	17 (24.3)	1 (25.0)	5 (22.7)	11 (25.0)	
No	53 (75.7)	3 (75.0)	17 (77.3)	33 (75.0)	
Internal mammary node irradiation					0.305
Yes	27 (38.6)	3 (75.0)	8 (36.4)	16 (36.4)	
No	43 (61.4)	1 (25.0)	14 (63.6)	28 (63.6)	
Supraclavicular node irradiation					0.330
Yes	57 (81.4)	4 (100)	16 (72.7)	37 (84.1)	
No	13 (18.6)	0 (0)	6 (27.3)	7 (15.9)	

Values are presented as number (%).
PMRT, postmastectomy radiation therapy; RT, radiotherapy; RH, reverse hockey stick.
[a)]Irradiated axillary level means number of irradiated axillary lymph node level. For example, 2 level means axillary level I–II or II–III.

80.0%, respectively. In the 1990 cohort, the pathological and molecular data were not available for a relatively large number of patients and most of patients received CMF chemotherapy, rather than anthracycline or taxane-based chemotherapy. In addition, in the 2000 cohort, all patients with HER2/neu (+) did not receive trastuzumab. Therefore, we conducted a survival analysis by era (Table 4). Except for the 10-year OS, all other treatment outcomes demonstrated improvement over the study period.

The available follow-up data for 700 patients revealed that 116 patients (16.6%) experienced recurrence. Recurrence at locoregional and distant sites decreased significantly over the study years: 24 (44.4%), 59 (23.5%), and 33 (8.4%) patients in 1990, 2000, and 2010, respectively ($p < 0.001$). The first recurrence site was locoregional recurrence (LRR) in 29 (25.0%), distant metastasis (DM) in 66 (56.9%), and LRR and DM in 21 (18.1%). Nine (12.9%) of 70 patients with PMRT and 107 (17.0%) of 630 patients without PMRT exhibited recurrences. Of nine patients with recurrences in PMRT group, LRR at their first recurrence was observed in one patient (1.4%). The LRR site was supraclavicular LN. In patients without PMRT, LRR at their first recurrence was present in 49 patients (7.8%). LRR was significantly lower in the PMRT group compared to the no-PMRT group ($p = 0.043$). In the PMRT group, 13 patients (18.6%) did not receive axillary irradiation. Among them, four patients had recurrence as DM (1 bone metastasis, 1 liver metastasis, and 2 lung metastases). There was no LRR. Detailed information on the recurrence sites in the PMRT group and the no-PMRT group is provided in Supplementary Table 1.

The 10-year LRRFS showed a trend toward improvement in the PMRT group compared to the no-PMRT group (98.6% vs. 88.8%, $p = 0.055$). However, there was no significant difference in 10-year OS, RFS, or DMFS between PMRT and no-PMRT groups (Table 5). Given the substantial differences in treatment approaches between patients in the 1990s and 2000s and those in more recent years, we further analyzed the impact of PMRT within the 2010 cohort. In 2010 cohort, PMRT was not associated with a significant survival benefit (Supplementary Table 2).

Table 4. Treatment outcomes by study era

	1990 (n = 54)	2000 (n = 251)	2010 (n = 395)	p-value
Recurrence				< 0.001
No	30 (55.6)	192 (76.5)	360 (91.1)	
Yes	24 (44.4)	59 (23.5)	33 (8.4)	
NA	0 (0)	0 (0)	2 (0.5)	
Locoregional recurrence	13 (24.1)	22 (8.8)	17 (4.3)	< 0.001
Distant metastasis rate	18 (33.3)	51 (20.3)	25 (6.4)	< 0.001
10-Year OS (%)	54.0	85.0	91.9[a]	0.077[b]
10-Year RFS (%)	54.7	75.1	89.8[a]	< 0.001[b]
10-Year LRRFS (%)	73.5	90.5	94.3[a]	0.049[b]
10-Year DMFS (%)	62.9	78.6	92.7[a]	0.002[b]

Values are presented as number (%) unless otherwise indicated.
OS, overall survival; RFS, recurrence-free survival; LRRFS, locoregional recurrence–free survival; DMFS, distant metastasis–free survival.
[a]Because the median follow-up period of the 2010 cohort was approximately 54 months (range, 2 to 69), the survival analysis results of the 2010 cohort are 5-year results.
[b]The p-value is for comparing the combined 1990 and 2000 cohorts against the 2010 cohort.

Table 5. Treatment outcomes by postmastectomy radiotherapy

	PMRT (n = 70)	No PMRT (n = 630)	p-value
Locoregional recurrence	1 (1.4)	51 (8.1)	0.043
Distant metastasis rate	8 (11.4)	86 (13.7)	0.598
10-Year OS (%)	79.0	81.6	0.738
10-Year RFS (%)	83.0	75.6	0.508
10-Year LRRFS (%)	98.6	88.8	0.055
10-Year DMFS (%)	84.3	79.6	0.754

Values are presented as number (%) unless otherwise indicated.
PMRT, postmastectomy radiotherapy; OS, overall survival; RFS, recurrence–free survival; LRRFS, locoregional recurrence–free survival; DMFS, distant recurrence–free survival.

In the current study, chemotherapy regimen was related to survival outcomes of the participating patients. Anthracycline-based chemotherapy significantly reduced the rates of LRR and DM compared to CMF chemotherapy ($p < 0.001$ and $p = 0.001$) (Table 6). Additionally, it led to significant improvements in 10-year OS, RFS, and LRRFS ($p < 0.001$, $p = 0.003$, and $p < 0.001$). Of 175 patients with positive HER2/neu status, treatment with trastuzumab improved 10-year RFS (94.7% vs. 66.2%, $p = 0.040$). There was no significant difference in 10-year OS for trastuzumab and no-trastuzumab groups (93.3% vs. 86.5%, $p = 0.609$).

Treatment-related complications were analyzed separately in the PMRT group and the no-PMRT group. Among the 70 patients who received PMRT, PMRT-related complications were evaluable in 63 patients: three patients (75.0%) in 1990, 20 patients (90.9%) in 2000, and 40 patients (90.9%) in 2010. In the 1990 cohort, PMRT-related complications was not observed. In the 2000 cohort, one patient (4.5%) developed grade 3 lymphedema. In the 2010 cohort, five patients (11.4%) experienced lymphedema (three with grade 1, while the remaining two had no reported grade information), and two patients developed grade 1 radiation pneumonitis. The most common PMRT-related complication was lymphedema. Axillary LN dissection, the number of dissected LNs, axillary LN irradiation, and the irradiated axillary node level were not associated with the development of lymphedema ($p = 0.999$, $p = 0.997$, $p = 0.999$, and $p = 0.995$, respectively).

In the no-PMRT group, treatment-related complications were evaluable in 398 patients: 39 patients (78.0%) in 1990, 125 patients (54.6%) in 2000, and 234 patients (66.7%) in 2010. No treatment-related complications were reported in the 1990 cohort. In the 2000 cohort, nine patients (7.2%) experienced treatment-related complications, including lymphedema in six patients (one with grade 2 and five with grade 1), neutropenia in three patients (one with grade 3, one with grade 2, and one with grade 1), and grade 3 nausea in one patient. In the 2010 cohort, treatment-related complications occurred in 30 patients (12.8%), including lymphedema in 23 patients (three with grade 2, 18 with grade 1, and two with no reported grade information), neutropenia in two patients (one with grade 1 and one with no reported grade information), cardiac complications associated with herceptin in two patients (both grade 2), web syndrome (grade 1) in one patient, pulmonary fibrosis in one patient (no reported grade information), and chest wall swelling in one patient (no reported grade information). The most common treatment–related complication was lymphedema. Axillary LN dissection and the number of dissected LNs were not associated with the development of lymphedema ($p = 0.306$ and $p = 0.998$, respectively).

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Table 6. Treatment outcomes by chemotherapy

	No CTx (n = 52)	CMF (n = 181)	Anthracycline-based CTx (n = 433)	p-value
Locoregional recurrence	6 (11.5)	26 (14.4)	17 (3.9)	< 0.001
Distant metastasis rate	8 (15.4)	39 (21.5)	43 (9.9)	0.001
10-Year OS (%)	54.7	75.3	91.2	< 0.001[a]
10-Year RFS (%)	63.8	72.5	78.3	0.003[a]
10-Year LRRFS (%)	83.5	84.6	94.1	< 0.001[a]
10-Year DMFS (%)	72.9	78.4	78.5	0.110[a]

Values are presented as number (%) unless otherwise indicated.
CTx, chemotherapy; CMF, cyclophosphamide, methotrexate, and fluorouracil; OS, overall survival; RFS, recurrence–free survival; LRRFS, locoregional recurrence–free survival; DMFS, distant metastasis–free survival.
[a]The p-value is for comparing CMF and anthracycline-based chemotherapy.

Discussion and Conclusion

We investigated the use of PMRT in patients with T1–2N1 breast cancer treated with mastectomy at 16 institutions in Korea over 2 decades. The number of patients for this study markedly increased in recent years, which represented the rise of incidence of breast cancer in Korea. PMRT was performed in about 10% of patients in the entire study population. The proportion of patients who received PMRT did not change significantly over 2 decades; however, PMRT utilization was profoundly varied (ranging from 0%–87.5%) among the participating institutions. PMRT was preferred for the patients with high-risk factors according to each institution's criteria. Radiation field and technique were different among the radiation oncologists. The majority of patients received anthracycline-based chemotherapy (66.8%) or CMF (27.9%). Despite the presence of high-risk features in patients receiving PMRT, 10-year LRRFS was higher in the PMRT group.

The benefits of PMRT in patients with T1–2N1 breast cancer following mastectomy remain controversial because of undetermined significance on the patient's survival and potential concerns of morbidity [4,6,16]. Several challenges complicate the assessment of PMRT outcomes. (1) Including this study, the patients who received PMRT were more likely to exhibit high-risk features; however, the definition of high-risk features varies across institutions, and the institutional criteria for administering PMRT in patients with a limited number of involved LNs remain unstandardized. (2) RT field and technique vary significantly institutions. While some institutions irradiate the chest wall and comprehensive LN area (axillary, supraclavicular, and internal mammary LN), others limit the treatment field to the chest wall alone or the chest wall with select LNs area. (3) Breast cancer is a disease with a long natural history. Based on Early Breast Cancer Trialists' Collaborative Group review on the effect of PMRT in the patients with N1 disease, who were followed up for 20 years, LRR in patients with N1 disease was shown to increase steadily for 10 years after mastectomy and RT reduced both recurrence and breast cancer mortality [17]. They reported that approximately one breast cancer-related death was avoided in the 20 years after RT for every 1.5 recurrences of any type (either locoregional or distant) avoided during the first 10 years after RT. Therefore, it is necessary to long-term follow-up for more than 10 years to determine the beneficial effects of PMRT on the survival outcomes in the patients with T1–2N1 breast cancer. Furthermore, a large number of subjects is required to draw a meaningful conclusion in the era of modern multimodality therapy.

Lately, the proportion of patients with more advanced features, such as T2 disease, three positive LNs, or LN size of ≥ 10 mm, have decreased significantly, and increased use of anthracycline-based chemotherapy over CMF has yielded favorable results. It has been shown that the emerging treatment strategies for breast cancer, such as taxane-based chemotherapy, endocrine therapy, and immune-oncologic agents tailored to subtype are associated with superior and more effective results [10,18]; therefore, the effect of PMRT on survival might be expected to decrease in the modern multimodal treatment era. Consistent with this, PMRT did not provide any survival benefit in the 2010 cohort (Supplementary Table 2).

In order to determine the patient groups that can truly benefit from RT, several investigators have attempted to identify the risk factors associated with the recurrence after mastectomy in the patients who did not receive PMRT. Young age and three positive LNs were associated with a significantly high risk of LRR, implying that PMRT may also be favorable to this group [11,19-21]. Furthermore, there might be patients with molecular features that are at high risks of LRR after mastectomy, and they may benefit from PMRT. The 21-gene recurrence score (RS) assay has been validated as an independent prognosticator of LRR, distant recurrence, and OS in women with node-positive estrogen receptor (ER)–positive breast cancer [22-24]. The 21-gene RS assay may therefore be useful as a predictive marker for potential OS benefit from PMRT in women

with T1–2N1 ER-positive breast cancer. Now, the Canadian Tailor RT trial (CCTG MA.39, NCT03488693) is underway on women with T1–2N1 disease and documented low RS who underwent breast-conserving surgery or mastectomy randomizing to either regional radiation or no regional radiation, with breast cancer recurrence-free interval as the primary objective. This trial can provide clarity regarding the value of RS as a predictor of the value of RT in women with T1–2 N1 breast cancer.

In summary, PMRT utilization in patients with T1–2N1 breast cancer following mastectomy did not change significantly over two decades in Korea. Despite the presence of high-risk features in those receiving PMRT, there was an improvement in the 10-year LRRFS of the PMRT group. Prospective randomized study with a large number of patients and long-term follow-up is necessary to determine the impact of PMRT on the survival outcomes and for the selection of the patients who may benefit from PMRT. Further research is needed to reflect the latest patterns of practice.

Statement of Ethics

This study protocol was reviewed and approved by the Korean Radiation Oncology Group (protocol No. KROG 14-21). The need for patients' informed consent was waived by each institutional review board because of the retrospective nature of the study.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Author Contributions

Data collection, MSK, SD, YBK, WP, SHP, IJL, BOC, JK, SJA, WSY, JHK, JHL, DK, HLP, YJK, SYL; Formal analysis and writing, MSK; Review and of the review and editing, KRP, SDA.

Data Availability Statement

The data that support the findings of this study are not publicly available due to their containing information that could compromise the privacy of research participants but are available upon request from the corresponding author.

Supplementary Materials

Supplementary materials can be found via https://doi.org/10.3857/roj.2025.00052.

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