Outcomes in patients with pT3N0M0 breast cancer with and without postmastectomy radiotherapy

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Abstract

Background The role of adjuvant postmastectomy radiotherapy (PMRT) remains controversial for patients with pT3N0M0 breast cancer after mastectomy, especially when patients were treated with the updated adjuvant chemotherapy and much more advanced radiation technology. The present analysis compared locoregional recurrence-free survival (LRFS), disease-free survival (DFS), and breast cancer-specific survival (BCSS) in pT3N0M0 patients treated with mastectomy, stratified by PMRT use.

Methods Between October 2000 and 8 September 2016, the database of the Breast Cancer Center of Shanghai yielded 114 patients with node-negative non-metastatic breast cancer with tumors >5 cm. Fifty-nine (51.8%) received adjuvant PMRT. Univariate and multivariate analysis were performed to assess the risk factors for survival. Differences between the two groups were compared using the log-rank test.

Results The median follow-up was 62.3 months. Five-year LRFS was 100% in the PMRT group vs. 98.1% in the non-PMRT group (P=0.17); 5-year DFS was 93.2% in the PMRT group vs. 90.5% in the non-PMRT group (P=0.40). Univariate analysis identified a family history of malignant tumors, lymphovascular invasion (LVI), or triple-negative breast cancer (TNBC) molecular subtype were associated with higher locoregional recurrence (LRR) (P<0.05); furthermore, patients who were estrogen receptor-negative (P=0.0593) or who had grade 3 histologic features (P=0.0776) tended to have a higher rate of LRR. No PMRT was the only risk factor independently associated with poorer DFS (P=0.042) on multivariate analysis. No difference in BCSS was observed between the two groups.

Conclusions The present study demonstrated a low LRR rate and good survival for node-negative breast cancer >5 cm. PMRT tended to improve LRFS and significantly improved DFS. Patients with risk factors including positive family history, TNBC subtype, LVI positivity, and grade 3 disease are at high risk for LRR and might benefit from PMRT.

Background

Breast cancer is the most commonly diagnosed malignancy in women and the second most commonly diagnosed cancer worldwide[1]. Post-mastectomy radiation therapy (PMRT) remains the most frequently used therapy for selected patients with breast cancer, with a survival benefit of local control and overall survival (OS)[2, 3]. According to the National Comprehensive Cancer Network (NCCN) guidelines for breast cancer, patients with positive lymph nodes after mastectomy were routinely recommended to undergo radiation therapy, but for those with negative lymph nodes, the indication of PMRT is still controversial[4].

In 2005, the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) demonstrated a reduced 5-year local recurrence rate (LRR) (6–2%) for node-negative patients who underwent PMRT, along with increased non-breast cancer mortality[5], while the radiotherapy techniques applied in the EBCTCG analysis were outdated and the database of patients included node-negative patients with pT1–2 and pT4.

According to the Surveillance, Epidemiology, and End Results (SEER) data analysis, the number of pT3N0M0 patients receiving PMRT has increased over time[6], from 22% reported between 1998–2002[6] to 42% between 2000–2010[7], and even more for younger patients (47% for those aged < 50 years from 1998–2007)[8]. Recent studies demonstrated nearly half of patients with pT3N0M0 diagnosis received PMRT[9, 10]. The MD Anderson Cancer Center indicated that 73.5% of cT3N0 and 64.0% of pT3N0M0 patients received PMRT[11].

Considering the cost and side effects of PMRT, it is important to define the role of PMRT for the pT3N0M0 subgroup in this new era of radiotherapy and identify those who can really benefit from PMRT in this setting. Many studies explored the role of PMRT in patients with breast cancer with a pathologic diagnosis of pT3N0M0, but the results were conflicting. Hence, we reviewed pT3N0M0 patients from our breast cancer database to better understand the biological behavior of this subgroup and to determine optimal treatment strategies for these patients.

Methods

Patient population

From 2000 to 2016, a total of 114 female patients with primary breast cancer diagnosed as pT3N0M0 were retrospectively reviewed in our study. All patients were treated with modified mastectomy with or without adjuvant therapy, including chemotherapy, hormonal therapy, and PMRT. Patients with a malignant cancer diagnosis beforehand, or with bilateral breast cancer at diagnosis, or who received neoadjuvant chemotherapy, and those with a follow-up time of less than 4 months were excluded. The review of data for this investigation was approved by the institutional review board of our center.

Treatments

All patients underwent modified mastectomy and 80.7% received adjuvant chemotherapy. The majority (73/92, 79.35%) of the patients received anthracycline-based chemotherapy, with approximately half (47/92, 51.1%) of the patients receiving a combination of anthracycline and taxane, while 13% (12/92) of the patients received taxane-based chemotherapy only. A small group (7/92, 7.61%) of patients received chemotherapies other than those mentioned above, with five of seven undergoing CMF (cyclophosphamide, methotrexate, 5-fluorouracil) treatment. Complete axillary lymph node dissection was performed in 95 (83.3%) patients, while sentinel lymph node biopsy was performed in 19 (16.7%) patients. The median number of lymph nodes dissected during surgery was 15. In total, 85.0% (51/60) of ER/PR positive patients received hormonal therapy with either tamoxifen or an aromatase inhibitor, while 56.8% (21/37) of patients who were HER2-positive were treated with trastuzumab.

Fifty-nine (59/114, 51.8%) patients received PMRT, while 55 (55/114, 48.2%) did not. When PMRT was used, a dose of 50 Gy in 25 fractions was delivered to the chest wall without regional nodal basins.

Statistical analysis

Locoregional recurrence (LRR) was defined as disease recurrence in the ipsilateral chest wall or the ipsilateral regional lymph nodal basins (axilla, internal mammary lymph node, supraclavicular fossa, or infraclavicular fossa). Distant metastasis (DM) was defined as disease recurrence other than at LRR sites. Disease-free survival (DFS) was defined as living without any LRR, DM events, or secondary malignant disease. Time to locoregional free survival (LRFS), DFS, and breast cancer-specific survival (BCSS) were calculated from the date of pathology diagnosis. Univariate analysis was used to assess the risk of all the variables to LRFS and DFS. Variables with a *P*-value of less than 0.2 and those reported as important in previous studies were included in a multivariate analysis. Because there was a low rate of LRR (2/114, 1.75%), multivariate analysis was not performed for LRFS. Survival was calculated by the Kaplan-Meier method and comparisons were performed using the log-rank test. The distribution of factors between groups was analyzed using the chi-squared method. *P*-values of less than 0.05 were considered statistically significant. Statistical analyses were performed using R package 3.6.2 (https://cran.r-project.org/).

Results

Patient and tumor characteristics

Of the 114 patients enrolled in the study according to the inclusion criteria, 59 (51.8%) received PMRT and 55 (48.2%) did not. The median follow-up time of patients was 62.3 (range, 4.6–211.7) months for the entire cohort, 61.9 months for the PMRT cohort, and 62.7 months for the non-PMRT cohort. Clinical and pathological characteristics of the patients are listed in Table 1. One patient in the PMRT group had positive margins. Younger patients were more likely to be offered radiation (*P*=0.002), while other variables were balanced between the two groups. Approximately 61.2% of premenopausal patients received PMRT (*P*=0.079), and more patients in the PMRT group had lymphovascular invasion (LVI) (27.1% vs 12.73%, *P*=0.210) or received adjuvant chemotherapy (84.7% vs 76.4%, *P*=0.071) compared with the non-PMRT group. Information regarding use of PMRT across different years is summarized in Figure 1, which showed a relatively stable trend from 2010.

LRR according to PMRT use

The 5-year cumulative LRFS was 98.1% in the non-PMRT cohort and 100% in the PMRT cohort. The cumulative survival of LRFS is plotted in Figure 2a according to PMRT use. PMRT improved LRFS for pT3N0M0 patients but did not reach statistical significance (*P*=0.17). Two LRR events occurred, both of which were in the non-PMRT cohort. Both events occurred in patients with triple-negative breast cancer (TNBC) molecular subtype, grade 3 pathologic features, and LVI positivity. One of the patients experienced relapse in the regional axillary lymph nodes 10 months after mastectomy, without simultaneous distant failure. This patient had a total of 10 lymph nodes removed at axillary dissection and had a relatively bigger tumor of 12 cm in diameter and received taxane-based chemotherapy without PMRT. The second patient had LRR in the chest wall and subclavicular lymph nodes with simultaneous distant failure in bone, pleura, and mediastinal lymph nodes 8 years after primary surgery. This patient

had 20 lymph nodes removed at axillary dissection and received adjuvant chemotherapy without PMRT. Both patients were alive at the last follow-up. No LRR event was observed after distant metastasis. We did not identify any events in the only patient in the PMRT group that had positive margins.

We performed a univariate analysis on LRFS (Table 2). Patients with a family history of malignant tumors had a poorer LRFS (P=0.0078; Fig. 2b). TNBC patients were at risk of higher LRR than non-TNBC patients, regardless of whether we defined HER2 ++ (immunohistochemical staining) as negative (P=0.0062; Fig .2c) or positive (P=0.0014; Fig. 2d). Furthermore, if we divided patients into three subtypes, patients with luminal or HER2-positive subtypes had better LRFS than TNBC patients (P=0.023 and P=0.035; Fig. 2e and Fig. 2f, respectively). ER positivity seemed to be a protective factor for LRFS in pT3N0M0 patients (P=0.059; Fig. 2g). The univariate analysis showed grade 3 histologic features (P=0.078; Fig. 2h) and LVI positivity (P=0.0039; Fig. 2i) were unfavorable prognostic factors for LRFS. Because of the rarity of LRR events, multivariate analysis was not performed for LRFS.

DFS according to PMRT use

Five-year DFS was 90.5% in the non-PMRT cohort, and 93.2% in the PMRT cohort (P=0.40). Among the 12 patients with disease recurrence during follow-up, seven patients had second primary malignant tumors, two patients had LRR, and four patients developed distant metastasis (three in the non-PMRT group and one in the PMRT group). The only distant metastasis after PMRT occurred in bone at 40.7 months after primary surgery and this patient had luminal disease, dying of breast cancer 2 years later. She was 30 years old at diagnosis and had a total of 22 lymph nodes removed at axillary dissection, undergoing hormonal therapy and adjuvant chemotherapy based on anthracycline and taxane. Among the three patients with distant metastasis in the non-PMRT cohort, one had simultaneous LRR and has been described before, and the other two patients both suffered lung metastasis, with one having mediastinal lymph node involvement. A total of 17 and 18 lymph nodes were removed at axillary dissection in the two patients with lung metastasis. The patient who developed DM 12.1 months after primary surgery died of breast cancer approximately 2 years later, while the other patient who developed DM 8.3 years after primary surgery was still alive at last follow-up. Both patients received hormonal therapy and adjuvant chemotherapy based on anthracycline and taxane. The former had grade 3 histological features and was HER2-positive, undergoing two cycles of trastuzumab treatment.

We performed a multivariate analysis of DFS with factors reported to be important in the clinical setting (Table 3), and identified PMRT as the only independent favorable factor in DFS (P=0.042; Fig. 3).

Cumulative survival of BCSS

Five-year BCSS was 97.9% in the non-PMRT group and 96.3% in the PMRT cohort. The BCSS curves for the PMRT and non-PMRT cohorts overlapped with each other, with no differences observed (P=0.92).

Discussion

The application of PMRT in patients with pT3N0M0 breast cancer is controversial. Floyd et al.[12] assessed the value of PMRT in patients with node-negative breast tumors of 5 cm or larger. They found a low 5-year LRR rate of 7.6% (95% confidence interval, 3%–16%) and 5-year DFS of 86% in the cohort and demonstrated LVI as a risk factor for worse LRFS, DFS, and OS. Taghian et al. reviewed patients with tumors larger than 5 cm who were treated in five NSABP node-negative trials, and identified locoregional failure in 7.2% of patients with tumors of more than 5 cm [13]. In our study, the 5-year LRR rate was only 1.9% and 5-year DFS was 90.5% in the non-PMRT group, better than the findings in prior studies. Moreover, the risk of LRR at 5 years in patients treated with PMRT was even lower at 0%. The two abovementioned studies included patients between 1981 and 2002. However, in our study, seven of 28 patients (25%) treated between 2000–2008 received adjuvant chemotherapy, while 44 of 86 (81.9%) patients treated during 2009–2016 received adjuvant chemotherapy. Anthracycline-based adjuvant chemotherapy was delivered to 57.1% of patients during 2000–2008, while anthracycline- and taxane-based adjuvant chemotherapy was administered to 52.3% of patients during 2009–2016. Moreover, the application of trastuzumab in HER2-positive patients increased from 0% before 2008 to 56.8% after 2008, and hormonal therapy in ER-/PR-positive patients increased from 50% before 2008 to 93.8% after 2008. For patients who received PMRT mainly during 2009–2016, when systematic treatments were improved, it is very likely that the improvements in systematic treatment could have contributed to the lower rate of LRR and better DFS in our study. This could also partly explain why PMRT increased LRFS but without statistical significance. However, we must strengthen that for patients with risk factors, PMRT improved their LRFS and DFS and was found to be an independent prognostic factor for DFS.

Jagsi et al.[14] analyzed the failure rate in 877 node-negative patients treated by mastectomy without PMRT. They found the chest wall was the most common site of failure, and a tumor size greater than 2 cm, a margin less than 2 mm, premenopausal status, and LVI were significant prognostic factors. We only included patients with tumors of more than 5 cm, consistent with the results of Floyd et al. and Jagsi et al. LVI was also identified as an unfavorable factor, and, with more specific information, we also identified TNBC and a family history of malignant tumors as unfavorable prognostic factors. Two of three patients who had all three risk factors (TNBC subtype, grade 3, LVI +) developed LRR in our study. Taken together, we agree with the conclusions of Jagsi et al. that node-negative patients with high-risk factors should be recommended PMRT to improve locoregional control.

The three studies mentioned above did not compare survival difference between patients with or without PMRT. We could not identify whether PMRT would benefit pT3N0M0 patients from their data analysis. In 2017, a retrospective, multi-institutional review regarding PMRT for pT3N0M0 patients was reported with a median follow-up of 6.2 years and 5.3 years in the non-PMRT and PMRT cohorts, respectively[15]. In this study, there was an isolated local regional failure rate of 12% at 10 years without PMRT, and 5- and 10-year LRFS for the PMRT and non-PMRT cohorts were 98% and 88%, respectively (P=0.15)[15]. Consistent with their outcome, PMRT was also found to be associated with better locoregional control, but without statistical significance in our study (P=0.17). This might be because of the number of patients, and, more importantly, the number of events was relatively small in our study. However, we identified PMRT as an independent prognostic factor for DFS (P=0.042). In a study by Goulart et al.[16]

that included 100 patients with pT2=5.0 cm and pT3 >5.0 cm tumors treated by mastectomy, a low LRR rate (2.3% in the PMRT group vs 8.9% in the non-PMRT group) was demonstrated, but, similar to our results, they found no significant improvement in LRFS and BCSS with PMRT, and concluded that PMRT should be considered for patients with grade 3 histologic features and patients without hormonal therapy. In our study, there was also a trend toward worse LRFS for patients with ER negativity and grade 3 histologic features.

Studies of pT3N0M0 patients in large populations at individual or multiple institutions have been lacking because of the infrequency of this clinical scenario, and thus many databases have been explored to analyze the features of this rare cohort. A study by Johnson et al.[7] analyzed 2525 patients treated between 2000 and 2010 from the SEER database and found a benefit for PMRT. Multivariate analysis indicated that PMRT improved OS (HR 0.63, P<0.001) and cancer-specific survival (HR 0.77, P=0.045), and concluded that PMRT should be strongly considered in T3N0M0 patients. Cassidy et al.[17] analyzed data from National Cancer Data Base (NCDB) including 3437 patients with pT3N0M0 breast cancer who were initially treated by mastectomy between 2003 and 2011. They concluded that PMRT was found to be associated with improved OS (86.3% vs 66.4%, P<0.01), regardless of surgical margin status, tumor size, and receipt of systemic therapy. Francis et al.[10] analyzed the survival of 4291 pT3N0M0 patients from the NCDB and found improved OS for patients with PMRT on multivariate analysis (HR 0.72, P<0.001) and in the propensity score matching cohort (P<0.001). However, both the SEER database and NCDB had no records of LRR or detailed information regarding chemotherapy and hormonal therapy, NCDB even had no information on the cause of death, which might indicate that death from causes other than breast cancer may have contributed to the improved OS, as PMRT group had more younger patients in their studies. Another analysis of pT3N0M0 patients from the SEER database including patients less than 50 years old found no differences in BCSS and OS[8]. In our study, we did not find a significant difference in BCSS between the two groups. Altogether, all studies including ours demonstrated good survival for pT3N0M0 patients, especially in those who received PMRT.

In addition, during clinical practice, breast cancer is still commonly classified into different molecular subtypes according to immunohistochemical staining combined with the results of in situ hybridization analyses of human epidermal growth factor receptor 2 (HER2). Different subtypes represented diverse prognoses. In 2019, an analysis of the survival of 14,464 female patients with TNBC diagnosed with pT1-4N0M0 from the NCDB (2004–2014) was reported. In total, 801 patients were pT3N0M0, of which 51.6% received PMRT, application of PMRT was associated with better OS for patients with pT3 disease[9]. Additionally, multivariate analysis reported increased age, T stage, and positive surgical margins as negative variables for OS (5-year OS 62.6% vs. 74.3%, P<0.001)[9]. However, this study had a median follow-up of only 38.2 months (interquartile range, 25.9–51.7 months) and no survival data of LRFS and chemotherapy agents used; furthermore, the prognostic factors were analyzed among all patients including pT1–2 and pT4 patients[9]. There was no detailed information on basic characteristic distribution between pT3N0M0 TNBC patients with or without PMRT[9]. We had more specific information, and our study found TNBC patients suffered poorer LRFS and DFS compared with non-

TNBC patients or luminal subtypes. Thus, for pT3N0M0 patients with TNBC, especially among those with other risk factors, PMRT should be considered to improve outcomes.

Besides, a hypothesis has been proposed indicating that patients with breast cancer with a larger tumor volume (>5 cm) may represent a rare subgroup with benign biological behaviors[18]. In particular, a low LRR incidence was reported in previous studies, supporting the hypothesis indirectly. With the development of breast cancer classification by genotype and immunophenotype, the diagnosis for this rare cohort with pT3N0M0 breast cancer may be better interpreted. Patients who are at high risk may be distinguished from those who are not, thus avoiding unnecessary expenditure and toxicities from various treatments.

The main strength of our study is that it represents a relatively contemporary cohort of patients treated with modern radiation techniques and current systemic therapies. We were also able to obtain relatively specific clinical and pathologic information of patients. Conversely, one limitation is that, like all retrospective studies, it has selection bias and some missing information.

Conclusions

In conclusion, the results of our present study confirmed good survival for pT3N0M0 patients except for those with high-risk factors. PMRT significantly improved their DFS and was associated with better LRFS compared with non-PMRT patients. With contemporary systemic therapies, the 5-year LRR rate was low in patients treated with (0%) or without PMRT (1.9%), and thus PMRT should be considered for those with a number of high-risk factors, such as TNBC subtype, grade 3 histologic features, and LVI+. Studies stratified by genotype or immunotype as well as larger studies are warranted to better understand the biological characteristics and survival differences of this rare cohort. Individualization of radiation therapy may be indicated based on the different biological parameters.

Declarations

Ethics approval and consent to participate
An informed consent has been obtained from each patient before the treatment. The review of data for this investigation was approved by the institutional review board of our center.

Consent for publication
The institutional consent for publication has been granted by the Fudan University Shanghai Cancer Center. All authors have given the consent for publication.

Availability of data and materials
The data that support the findings of this study are available from the patient records of the Fudan University Shanghai Cancer Center, Shanghai, China; but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are

however available from the authors upon reasonable request and with permission of the Fudan University Shanghai Cancer Center, Shanghai, China.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

Chunyan Li analyzed and interpreted the patient data and was a major contributor in writing the manuscript. Miao Mo and Jing Yuan participated in gathering the original patient data. Jiangfeng Wang participated in gathering the updated part of the data. Xiaoli Yu, Xiaomao Guo and Xingxing Chen tutored the work and revised the manuscript. Other authors participated in the interpretation of the results. The authors read and approved the final manuscript.

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Abbreviations

ALND: axillary lymph node dissection; BCSS: breast cancer-specific survival; DFS: disease-free survival; DM: Distant metastasis; EBCTCG: Early Breast Cancer Trialists' Collaborative Group; ER: estrogen receptor; HER2: human epithelial growth factor receptor-2; HT: hormonal therapy; IDC: invasive ductal carcinoma; LRFS: locoregional recurrence-free survival; LRR: locoregional recurrence; LVI: lymphovascular invasion; NCCN: National Comprehensive Cancer Network; OS: overall survival; PMRT: postmastectomy radiotherapy; PR: progesterone receptor; SEER: Surveillance, Epidemiology, and End Results; TNBC: triple-negative breast cancer.

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Tables

Table 1. Patients' characteristics

	All patients (n = 114)		PMRT (n = 59)		No PMRT (n = 55)		
Characteristics	No.	%	No.	%	No.	%	P value
Age (years)							
Median(range)	53 (26-80)		50 (26-80)		57(28-78)		
< 50	41	35.96	29	49.2	12	21.8	0.002
≥ 50	73	64.04	30	50.8	43	78.2	
Family history							
Negative	99	86.8	51	86.4	48	87.3	0.896
Positive	15	13.16	8	13.6	7	12.7	
Menstrual status							
Premenopausal	49	42.98	30	50.8	19	34.5	0.079
Postmenopausal	65	57.02	29	49.2	36	65.5	
Pathology							
IDC	94	82.46	52	88.1	42	76.4	0.099
Other	20	17.54	7	11.9	13	23.6	
Tumor size (cm)							
Median (range)	6.0(5.1-16.0)		6.0(5.1-12.0)		6.0(5.1-16.0)		0.383
5.1-7.0	43	37.72	20	33.9	23	41.8	
> 7.0	71	62.28	39	66.1	32	58.2	
Grade							
I-II	58	50.88	32	54.24	26	47.27	0.968
III	42	36.84	23	38.98	19	34.55	
Unknown	14	12.28	4	6.78	10	18.18	
ALND							
≤ 15	58	50.9	27	45.8	31	56.4	0.258
>15	56	49.1	32	54.2	24	43.6	
ER							

Negative	46	40.4	22	37.3	24	43.6	0.432
Positive	65	57.0	36	61.0	29	52.7	
Unknown	3	2.63	1	1.69	2	3.64	
PR							
Negative	59	51.8	31	52.5	28	50.9	0.948
Positive	52	45.6	27	45.8	25	45.5	
Unknown	3	2.63	1	1.69	2	3.64	
HER2							
Negative	70	61.4	37	62.7	33	60.0	0.882
Positive	37	32.5	19	32.2	18	32.7	
Unknown	7	6.14	3	5.08	4	7.27	
Ki-67							
≤ 15%	30	26.32	18	30.5	12	21.8	0.798
> 15%	56	49.12	32	54.2	24	43.6	
Unknown	28	24.56	9	15.3	19	34.5	
Subtype							
Non-TNBC	90	78.95	47	79.7	43	78.2	0.990
TNBC	21	18.42	11	18.6	10	18.2	
Unknown	3	2.63	1	1.7	2	3.6	
LVI							
Negative	73	64.04	40	67.8	33	60.0	0.210
Positive	23	20.18	16	27.1	7	12.73	
Unknown	18	15.8	3	5.08	15	27.27	
Margin							
Negative	113	99.12	58	98.3	55	100	1.00
Positive	1	0.88	1	1.7	0	0.00	
Chemotherapy							
No	19	16.7	6	10.2	13	23.6	0.071
Yes	92	80.7	50	84.7	42	76.4	

Unknown	3	2.60	3	5.08	0	0	
Herceptin in HER2+patients							
No	16	43.2	9	47.4	7	38.9	0.603
Yes	21	56.8	10	52.6	11	61.1	
HT in ER/PR+ patients							
No	9	15.0	3	9.7	6	20.7	0.292
Yes	51	85.0	28	90.3	23	79.3	

PMRT, post-mastectomy radiotherapy; IDC, invasive ductal carcinoma; ALND, axillary lymph node dissection; ER, estrogen receptor; PR, progesterone receptor; HER2, human epithelial growth factor receptor-2; TNBC, triple-negative breast cancer; LVI, lymphovascular invasion; HT, hormonal therapy.

Table 2. Univariate analysis of LRFS

Variables	P value
Family history (Negative vs Positive)	0.0078
ER status (Negative vs Positive)	0.0593
Subtype (TNBC vs Non-TNBC)	0.0062
Subtype (HER2++ as positive) (TNBC vs Non-TNBC)	0.0014
Subtype (TNBC vs Luminal vs HER2+)	0.0235
Subtype (TNBC vs Luminal)	0.0354
PMRT (No vs Yes)	0.1701
Grade (I-II vs III)	0.0776
LVI (Negative vs Positive)	0.0039

ER, estrogen receptor; TNBC, triple-negative breast cancer; HER2, human epithelial growth factor receptor-2; PMRT, post-mastectomy radiotherapy; LVI, lymphovascular invasion.

Table 3. Multivariate analysis of DFS

Variables	P value
Family history (Negative vs Positive)	0.093
Menstrual status (premenopausal vs postmenopausal)	0.415
Age (≥ 50 vs < 50)	0.350
Tumor size (cm) (5.1-7 vs > 7)	0.651
Grade (I-II vs III)	0.113
LVI (Negative vs Positive)	0.429
ALND (> 15 vs ≤15)	0.252
Subtype (TNBC vs Non-TNBC)	0.252
ER status (Negative vs Positive)	0.653
PR status (Negative vs Positive)	0.678
HER2 status (Negative vs Positive)	0.638
PMRT (No vs Yes)	0.042

LVI, lymphovascular invasion; ALND, axillary lymph node dissection; TNBC, triple-negative breast cancer; ER, estrogen receptor; PR, progesterone receptor; HER2, human epithelial growth factor receptor-2; PMRT, post-mastectomy radiotherapy.
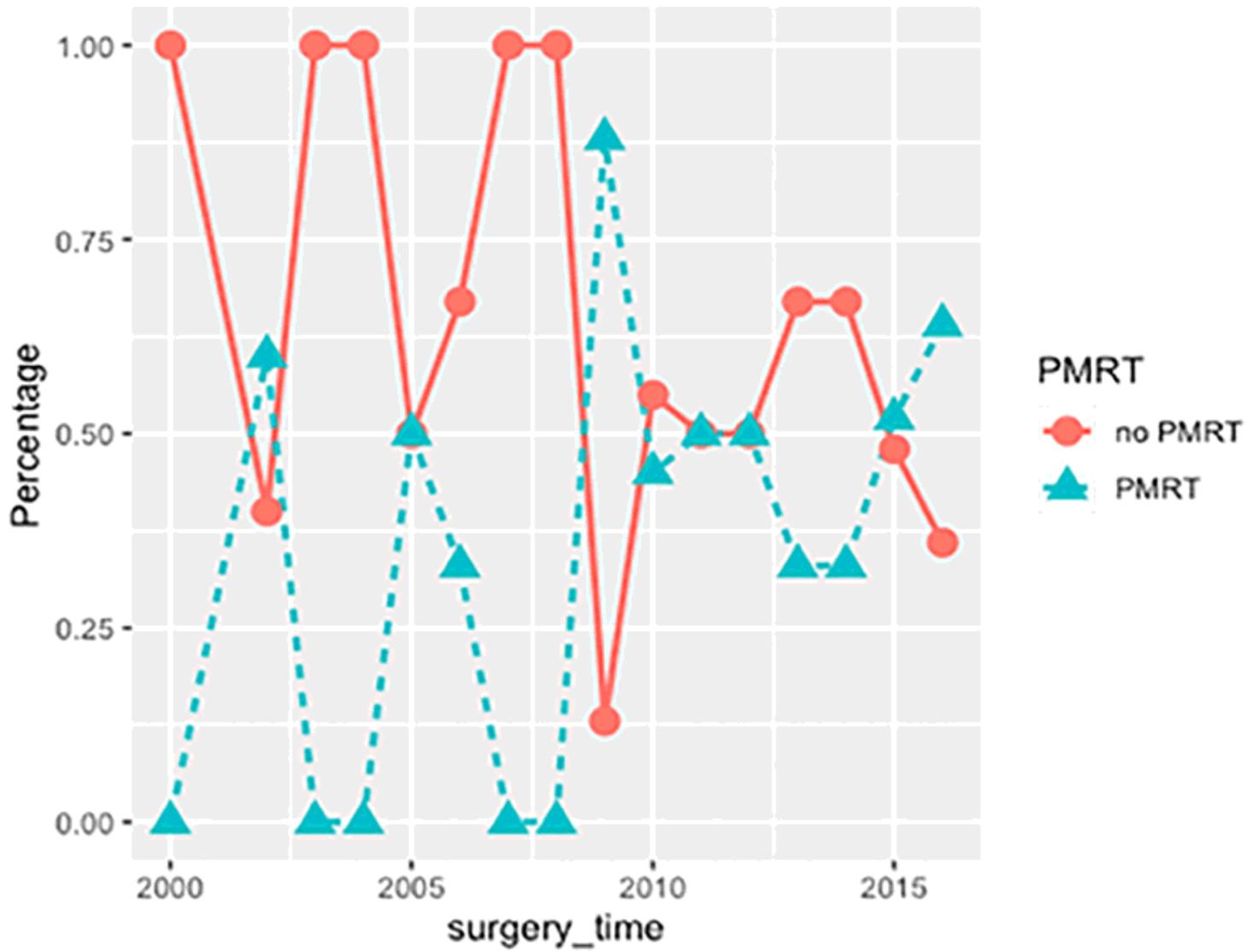
Figures

Figure 1

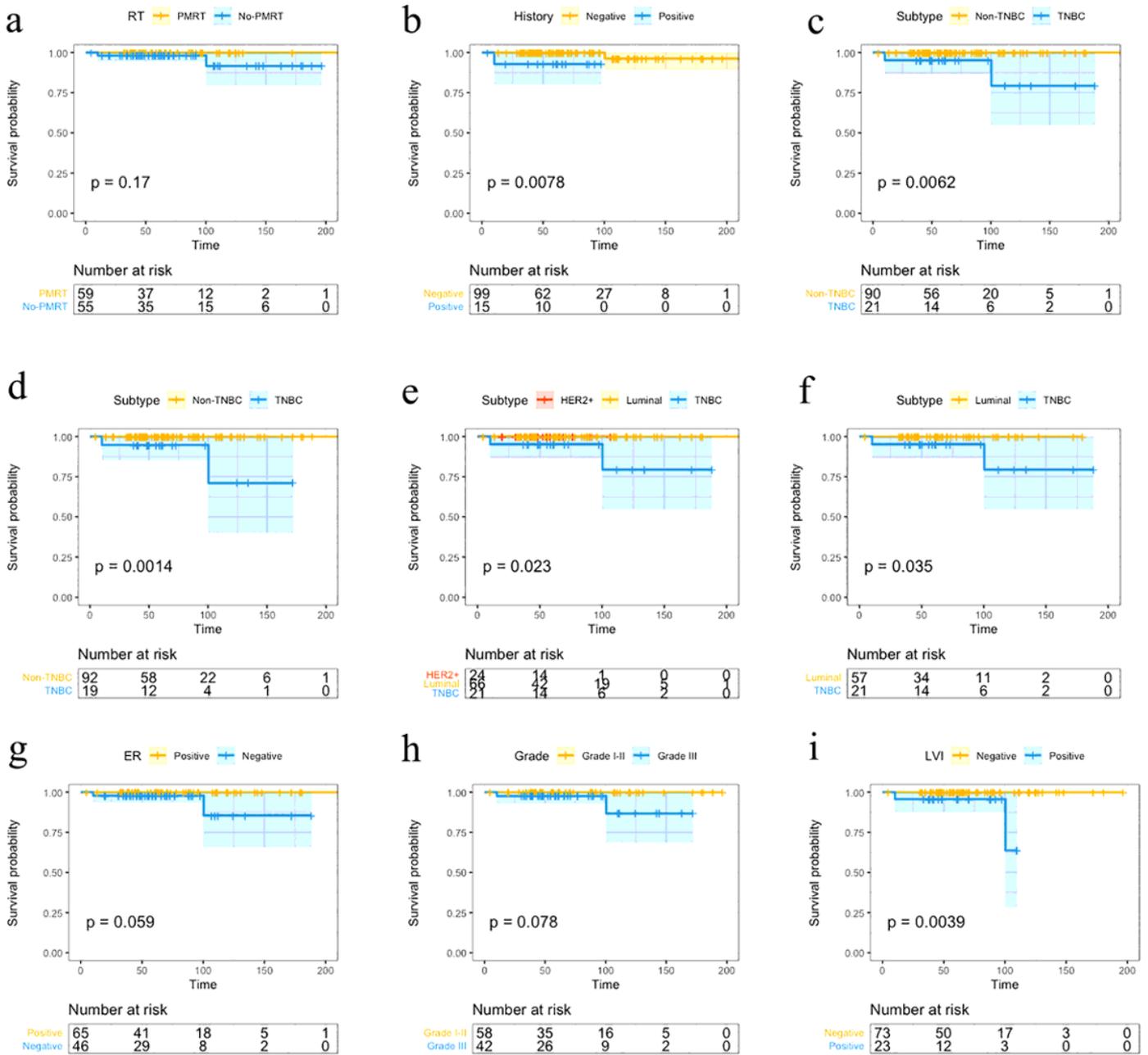Distribution of PMRT use according to year

Figure 2

LRFS of patients with pT3N0M0 breast cancer according to different variables. (a) LRFS according to PMRT. (b) LRFS according to family history. (c–f) LRFS according to molecular subtype. (g) LRFS according to ER status. (h) LRFS according to histologic grade. (i) LRFS according to LVI status.
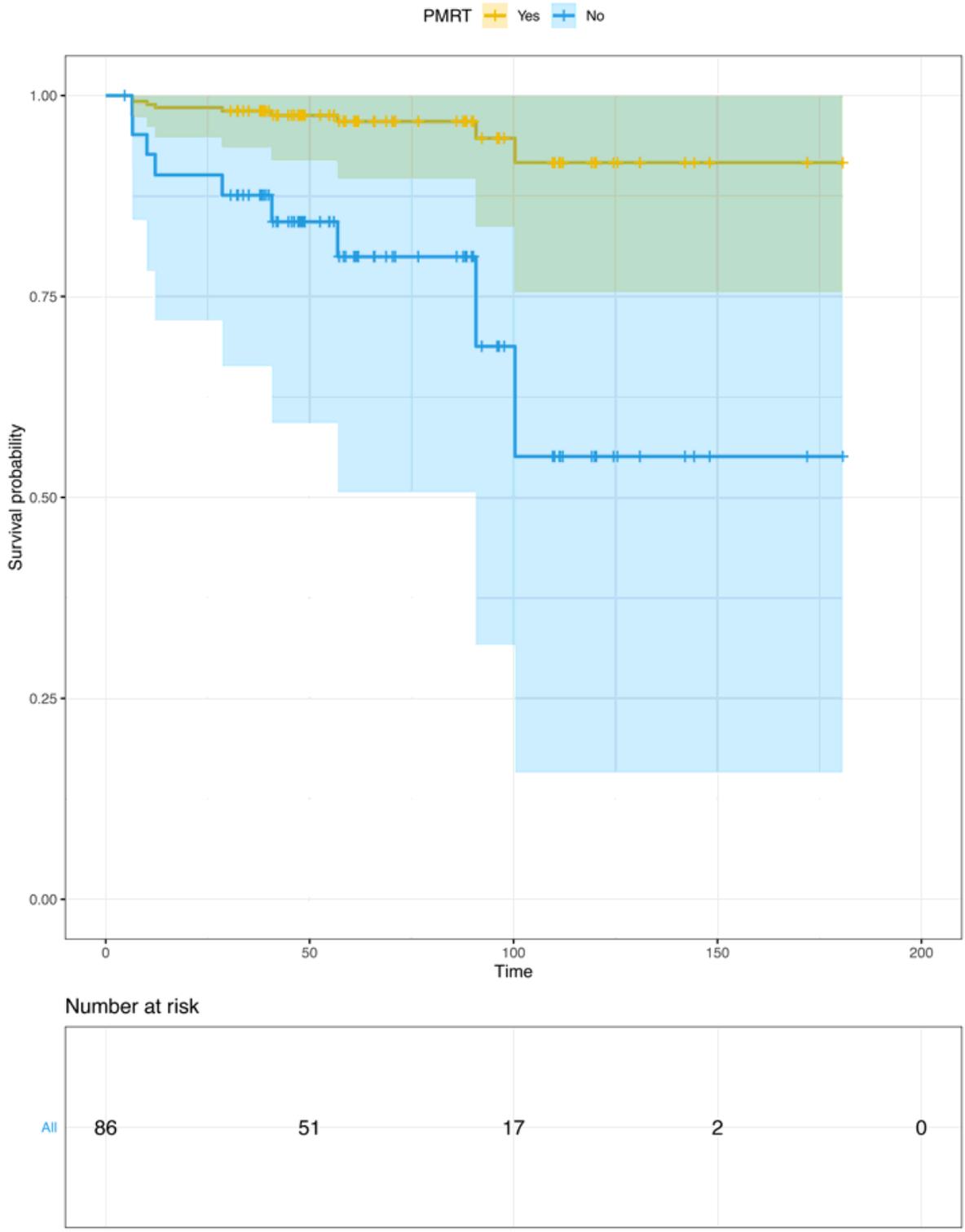
Figure 3

DFS according to PMRT use (after balancing by other variables in multivariate analysis)