Systematic Review

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Does Post-Mastectomy Radiotherapy Confer Survival Benefits on Patients With 1-3 Clinically Positive Lymph Nodes Rendered Pathologically Negative After Neoadjuvant Systemic Chemotherapy: Consensus from A Pooled Analysis?

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ABSTRACT

The advent of taxane-based chemotherapy has revolutionized breast cancer care. This advance has helped improve the response to downstaging tumors that might otherwise be inoperable. It has also helped in rendering clinically (cN+) positive lymph nodes (LNs) pathologically negative (ypN0). The standard of care for cN+ patients included post-mastectomy radiotherapy (PMRT), regardless of the response to neoadjuvant chemotherapy. However, PMRT in patients with 1–3 positive LNs still lacks definitive guidelines. Numerous retrospective results have been inconclusive about the benefit of PMRT on survival in patients with 1–3 positive LNs. This pooled analysis attempts to reach a consensus. The PubMed database was searched through October 2023. The search yielded 27 papers, of which 11 satisfied the inclusion criteria. The locoregional recurrence-free survival (LRRFS), disease-free survival (DFS), and overall survival (OS) for each study were tabulated when given, and two groups were created, the PMRT and NO PMRT, respectively. The results were then pooled for analysis. The total number of patients was 8340, 4136 in the PMRT group, and 4204 in the NO PMRT group, respectively. The LRRFS, DFS, and OS were 96.9%, 82.1%, and 87.3% for the PMRT group and 93.2%, 79.6%, and 84.8% for the NO PMRT group, respectively. There was no statistical significance in LRRFS, DFS, or OS between the two groups (p = 0.61, p = 0.61, and p = 0.38, respectively). PMRT does not seem to confer survival benefits in patients with pN1 rendered ypN0 for stages T1-3. This pooled analysis's findings should be confirmed prospectively with a longer period of follow-up.

Keywords: Post-mastectomy radiotherapy; neoadjuvant chemotherapy; regional nodal irradiation; clinically positive lymph nodes; pathological complete response

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Key Points

- Taxane-based neoadjuvant chemotherapy has improved response to downstaging and pathological complete response.
- The benefits on survival of post-mastectomy radiotherapy (PMRT) in breast cancer patients with T1-3 and 1-3 positive lymph nodes rendered pathologically negative post-neoadjuvant chemotherapy is not yet established.
- PMRT does not seem to confer survival benefits on breast cancer patients with T1-3 and 1-3 positive lymph nodes rendered pathologically negative post-neoadjuvant chemotherapy.
- Long-term follow-up of patients for 10 years or more is essential to determine the effect of forgoing PMRT on locoregional recurrence.
- Clinicopathological factors such as age, lymphovascular invasion, and tumor size have to be taken into consideration before forgoing PMRT.
- Ongoing prospective studies will determine the basis of radiotherapy administration in these specific groups.

Introduction

The role of post-mastectomy radiotherapy (PMRT) in patients with more than four positive lymph nodes (LNs) has been shown to improve survival. These trials have also shown improvement regardless of tumor size or the number of positive LNs (1). However, the benefit to low-tumor burden LNs (1–3 positive LNs) was debated due to these trials being based on the pre-taxane and human epidermal growth factor receptor 2 (HER2) targeted therapy eras. In addition, some studies

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indicated that these patients demonstrated a low rate of LRR (2, 3). In a series from the Cleveland Clinic, a 10% locoregional recurrence (LRR) rate was reported among patients with 1–3 positive LNs treated with mastectomy and chemotherapy without radiation (4). Other studies placed the LRR rate in the range of 4–10% (5, 6). However, in patients less than forty years of age with lymphovascular invasion (LVI), the five-year LRR rate was 24.3% (7). It is imperative that long-term follow-up be implemented, as 95% of LRRs occur within 10 years after surgical intervention (8).

The conflicting results and lack of evidence led the National Comprehensive Cancer Network to recommend that PMRT be "strongly considered" in patients with 1–3 positive LNs while also taking into account other clinical characteristics, such as life expectancy, age, comorbidities, tumor size, and LVI (9). Furthermore, a joint panel comprised of the American Societies of Clinical, Radiation, and Surgical Oncology recommended PMRT in patients with 1–3 positive LNs and T1-2 as the benefits outweigh the potential toxicities (10).

The advent of taxane-based chemotherapy has revolutionized breast cancer (BC) management. This advance has become a first-line treatment for responders, achieving a higher percentage of pathological complete response (pCR) in both the breast and axilla. Moreover, the addition of anti-HER2 therapy became standard due to its survival benefits (11, 12). The de-escalation in the management of the axilla both surgically and medically is made possible in such patients.

PMRT can lead to numerous side effects, both early and late after treatment. Early side effects, which occur weeks to months apart, can include skin thickening, pleural effusion, and radiation-induced pneumonia. The intermediate to late period, which can take months to years, includes breast fibrosis, pulmonary fibrosis, and fracture of overlying bone, among others (13).

The role of PMRT in the setting of adjuvant therapy has been shown to provide survival benefits for BC patients with positive LNs (1). However, the role of NAC on survival in patients with cN+ is yet to be determined. A prospective trial that is ongoing, namely the NSABP B51/RTOG 1304 (14), has recently presented the five-year results at the San Antonio Breast Cancer Symposium in December 2023 (SABCS) (15). This randomized clinical trial investigated if regional nodal irradiation (RNI) post mastectomy or the addition of regional nodal radiotherapy to whole breast radiotherapy post breast-conserving surgery (BCS) reduced invasive BC recurrence-free interval as a primary endpoint in patients with pathologically positive axillary nodes who are ypN0 after neoadjuvant chemotherapy. The secondary endpoints included LRR-free interval, distant recurrence-free interval, disease-free survival (DFS), and overall survival (OS). The current pooled analysis attempts to answer the question of the survival benefits of PMRT in patients with 1-3 positive LNs and clinical stage T1-3 rendered ypN0 post-NAC.

Materials and Methods

The PubMed database was searched through October 2023. The terminologies used were PMRT, cN+, ypN0, and NAC. The study cohort was required to encompass both cN+ and ypN0. The inclusion criteria were studies that looked at patients who had clinically positive LNs (1-3) and were rendered ypN0 post-neoadjuvant systemic chemotherapy with rates given for either the locoregional recurrence-free survival (LRRFS), DFS, or OS. Exclusion criteria encompassed studies that dealt solely with BCS, whole breast radiotherapy, RNI, and tumor stage T1-4. The data was collected, and patients were then divided into two groups, each exclusively made up of cN+ and ypN0 post-NAC: PMRT and NO PMRT. When given, the number of patients who had RNI was recorded as part of the PMRT group. The number of patients for LRRFS, DFS, and OS rates was calculated for each study when given. The results were then pooled for analysis. A chi-square test with Yates's correction was applied. Confidence intervals (CI) were determined based on a non-central chi-square distribution for Q (a common effect measure). The pooled mean follow-up period was calculated. Subgroup pooled analysis of LRRFS, DFS, and OS was carried out for T1-2 and T2-3 studies, respectively, and the *p*-values were tabulated.

Results

The PubMed search yielded 27 studies in total. Ten were eliminated due to dealing with stage T1-4, BCS, comparison of ypN0 to ypN1, whole breast radiotherapy, survival by subtype, and survival data for regional LN irradiation only. Seventeen were initially found to satisfy the criteria. Five more were eliminated due to incomplete data (Figure 1). The studies included were (16-26). The total number of patients was 8340, with a pooled mean follow-up period of 6.3 years and there were 4136 patients in the PMRT (RNI) group and 4204 patients in the NO PMRT group (Table 1). RNI was included as part of the PMRT in all of the studies. Only five studies gave a breakdown (18, 19, 21, 22, 25). The LRRFS, DFS, and OS were 96.7% (95% CI: 96.5–96.9), 82.1% (95% CI: 81.0–83.2), and 87.3% (95% CI: 86.9–87.7) for the PMRT group, and 93.9% (95% CI: 93.6–94.2), 79.6% (95% CI: 78.7–80.5), and 84.8% (95% CI: 84.3–85.3) for the NO PMRT group, respectively. Some studies did not report figures for LRRFS (17, 19, 23-25) and DFS (22-24). There was no significant

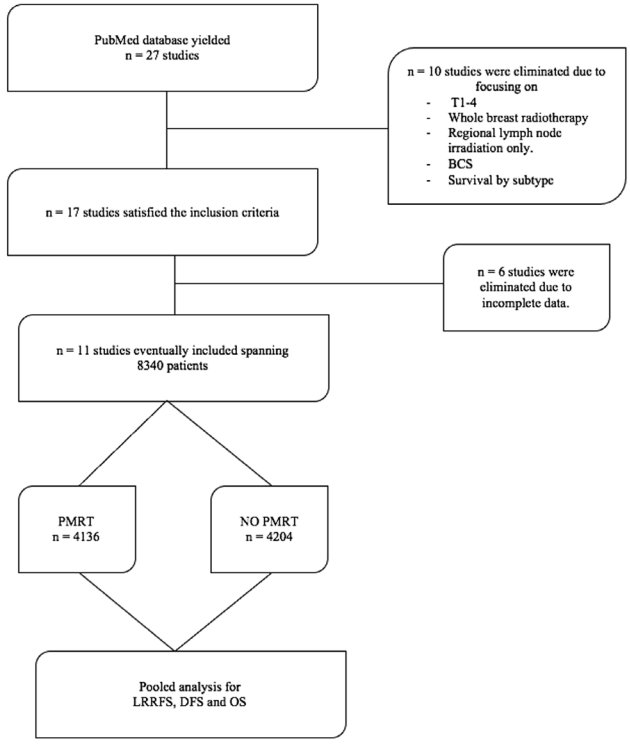

Figure 1. CONSORT flow diagram showing study distribution

PMRT: Post-mastectomy radiotherapy; LRRFS: Locoregional recurrence-free survival; DFS: Disease-free survival; OS: Overall survival; BCS: Breast-conserving surgery

difference between the two groups for LRRFS, DFS and OS at p = 0.61, p = 0.61, and p = 0.38, respectively. The subgroup analysis of the T-stage (Tables 2, 3) also showed no significant differences in LRRFS, DFS, or OS for T1-2 and T2-3 for both groups (Table 4).

Discussion and Conclusion

This pooled analysis included 8340 patients with a pooled mean follow-up period of 6.3 years. The results for survival are in agreement with most of the literature. However, a longer follow-up period of 10 years or more is essential to validate these results, as 95% of LRRs occur within 10 years after surgical intervention (8). Furthermore, LRRFS, DFS, and OS subgroup analysis was performed for T1-2 and T2-3, which also showed no statistical significance. The LRR for the PMRT group in this study was 3.3% and 6.1% for the NO PMRT group, respectively, which are within the reported rates. Only two studies (20, 21) gave 10-year LRR rates, which were 4% *vs.* 7% (study 19) and 2.5% *vs.* 6.5% (study 20) for PMRT *vs.* NO PMRT, respectively. The administration of PMRT in patients who are cN+ and convert to ypN0 post-modern-era NAC remains challenging. Recommendations for PMRT are based on clinical stage and LN status (9, 27). These guidelines are based on the outcomes of randomized trials and patterns of failures (28-30). Patients who achieve pCR in the breast and axilla have a significantly decreased risk of LRR (31). Therefore, patients who are rendered ypN0 are effectively down-staged and might not benefit from PMRT (32). Modern-era NAC has been proven to improve LRR rates in the adjuvant role. McBride et al. (33) looked at patients in two eras and retrospectively analyzed the LRR rates in 1027 patients with T1-2 BC with 1-3 positive LNs treated with mastectomy and adjuvant chemotherapy with or without PMRT during an early era (1978–1997) and a later era (2000–2007). These eras were selected because they represented periods before and after the routine use of sentinel LN surgery, taxane chemotherapy, and aromatase inhibitors. 19% of the 505 patients treated in the early era and 25% of the 522 patients in the later era received PMRT. Patients who received PMRT had significantly higher-risk disease features. PMRT reduced the rate of LRR in the early-era cohort, with 5-year rates of 9.5% without PMRT and 3.4% with PMRT, and 15-year rates of 14.5% versus 6.1%, respectively. However, PMRT did not appear to benefit patients treated in the later cohort, with 5-year LRR rates of 2.8% without PMRT and 4.2% with PMRT. They stated that the risk of LRR for patients with T1-2 BC with 1-3 positive LNs treated with mastectomy and systemic treatment is highly dependent on the era of treatment. Modern treatment advances and the selected use of PMRT for those with high-risk features have allowed for the identification of a cohort at very low risk for LRR without PMRT. Miyashita et al. (34) enrolled patients who received NAC and mastectomy for cT1–4 cN0–2 M0 BC. They evaluated the association between radiotherapy and outcomes of LRR, distant DFS, and OS based on ypN status by multivariable analysis of 3326 patients. Multivariable analysis demonstrated that use of radiotherapy was independently associated with improved LRR for ypN2–3 patients only. The association between radiotherapy and OS was not statistically significant among ypN0 (p = 0.22) and ypN1 patients (p = 0.51). The results from this Japanese nationwide database study did not show significant associations between PMRT and improved survival among ypN0 and ypN1 patients and concluded that radiotherapy may be beneficial only for ypN2–3 BC patients who receive NAC and mastectomy in the modern era. However, another study carried out retrospectively concurred with the lack of benefit of PMRT for patients who achieve ypN0 but disagrees on its possible omission in patients with ypN1 (35). The current pooled analysis is for patients who achieve ypN0, and the results are in agreement for this group of patients.

It was not possible to carry out subgroup analysis for the different molecular subtypes in this pooled analysis due to inadequate data presentation. There are, however, conflicting findings in relation to the benefits of PMRT on subtypes. Cho et al. (18) looked at the benefit of PMRT in ypN0 patients after NAC according to molecular subtypes. They concluded that in patients who achieve ypN0 following NAC and mastectomy, PMRT shows no additional survival benefits for any molecular subtype. However, in another study, it was suggested that among ypN0 patients, only triple-negative breast cancer (TNBC) patients might benefit from PMRT (36). Furthermore, Miyashita et al. (34) suggested that radiotherapy significantly improved the LRR rate only for patients with HER2+ disease in their analysis, and patients with TNBC exhibited a higher LRR rate after NAC and mastectomy regardless of the presence or absence of PMRT. They also observed favorable LRR rates for HR+ patients in both groups. Although they indicated that high-risk subgroups for recurrence, such as those with TNBC and large tumors, are recommended for radiotherapy, their assessment needs further confirmation due to the small sample size. Factors that have also been found to influence LRR in those not receiving PMRT were positive margins, extracapsular extension, age less than forty, and LVI (19, 31, 37, 38). In further analysis, Muhsen et al. (19) examined the relationship between age, LVI presence, and LRR in patients who did not receive PMRT. They found that at 10 years, LRR rates for patients with no LVI and age >40 years were 2% (95% CI, 0.7–3.8), compared with 28% (95% CI, 11.0–22.1) in patients with LVI and age <40 years (p<0.0001). Tumor size has also been implicated as a LRR determinant, with higher rates of LRR seen in tumors ≥2 cm (39). Furthermore, PMRT in patients treated with taxane-based chemotherapy showed no benefit in LRRFS, DFS, or OS (21). Therefore, these LRR factors have to also be taken into account in the context of the type of chemotherapy used.

The addition of RNI to PMRT appears not to influence the LRRFS. Tam et al. (22) included patients treated with chest wall (CW) irradiation alone and CW with RNI. There was no benefit identified with RNI versus CW irradiation alone. Similarly, for BCS, Schlafstein et al. (40) compared the survival of whole breast (WB) radiotherapy alone with WB+ RNI. They found that the 10-year survival for WB alone versus WB + RNI was 83.6% and 79.5%, respectively (p = 0.14) and concluded that for women with cN1 BC who convert to ypN0 following NAC and BCS with SLNB alone, more extensive RNI may not provide a long-term survival benefit. Other trials have demonstrated benefits to DFS and decreased cancer mortality with extensive radiation in the modern era NAC (41, 42). A recently published meta-analysis by the Early Breast Cancer Trialists' Collaborative Group supports this notion. The meta-analysis was carried out on individual patient data from 14324 patients in 16 trials looking at radiotherapy to regional nodes in early BC. They reported that in the newer trials (12167 patients), which started during 1989-2008, RNI significantly reduced distant recurrence and BC mortality with no significant effect on non-BC mortality. However, in the older trials (2157 patients) during 1961–1978 RNI did not have a significant impact on recurrence. They concluded that these contrasting findings could reflect radiotherapy improvements since the 1980s (43).

Table 1. Pooled analysis of survival for all studies

	Author (year)	cN+ rendered ypN0 post NAC patients *n* =	Stage	ypN0 PMRT+(RNI) patients *n* = LRRFS/DFS/OS (%) patients *n*ˆ =	ypN0 NO PMRT patients *n* = LRRFS/DFS/OS % patients *n*ˆ =
Retrospective	Dai et al. (16) (2023)	116	1-2	31 -/90.2/96.7 *n* = 0/28/30 (5 year)	85 -/93.7/97.3 *n* = 0/80/83 (5 year)
Retrospective	Wang et al. (17) (2020)	142	1-2	110 94.5/88.7/96.1 *n* =104/98/106 (5 year)	32 90.1/72.4/95.0 *n* = 29/23/30 (5 year)
Retrospective	Cho et al. (18)* (2019)	189	1-3	111 (98) -/76.9/89.6 *n* = 0/85/99 (5 year)	78 -/77.5/88.9 *n* = 0/60/69 (5 year)
Retrospective	Muhsen et al. (19) (2018)	1087	1-2	163 (150) 96/75/81 *n* = 156/122/132 (10 year)	924 93/73/80 *n* = 859/675/739 (10 year)
Retrospective	Zeidan et al. (20) (2018)	684	1-2	337 97.5/77.3/81.7 *n* = 329/261/275 (10 year)	347 93.5/75.9/78.3 *n* = 324/263/272 (10 year)
Retrospective	Kim et al. (21) (2017)	714	1-2	130 (All) 97/94/98 *n* =126/122/127 (5 year)	584 96/90/96 *n* = 561/526/561 (5 year)
Retrospective	Tam et al. (22) (2017)	523	1-3	206 (146) -/-/86 *n* = 0/0/177 (10 year)	317 -/-/84 *n* = 0/0/266 (10 year)
Retrospective	Rusthoven et al. (23) (2016)	3040	1-3	1962 -/-/88.3 *n* = 0/0/1732 (5 year)	1078 (no PMRT) -/-/84.8 *n* = 0/0/914 (5 year)
Retrospective	Liu et al. (24) (2016)	1560	2-3	903 -/-/84.6 *n* = 0/0/764 (5 year)	657 -/-/81.7 *n* = 0/0/537 (5 year)
Retrospective	Shim et al. (25) (2014)	151	2-3	105 (All) 98.1/91.2/93.3 *n* = 103/96/98 (5 year)	46 92.3/83.0/89.9 *n* = 42/38/41 (5 year)
Retrospective	Le Scodan et al. (26) (2012)	134	2-3	78 96.2/79.2/88.3 *n* = 75/62/69 (5 year)	56 92.5/85.2/94.3 *n* = 52/48/53 (5 year)
Total		8340		4136 *n* = 893*/874#/3609 % (96.7/82.1/87.3)	4204 *n* = 1867*/1713#/3565 % (93.9/79.6/84.8)

PMRT: Post-mastectomy radiotherapy; LRRFS: Locoregional recurrence-free survival; DFS: Disease-free survival; OS: Overall survival; NAC: Neoadjuvant chemotherapy; *: Number of patients for Studies with no LRRFS were deducted for PMRT 4136-3213 = 923 and for NO PMRT 4204 - 2215 = 1989; #: Number of patients for studies with no DFS were deducted for PMRT 4136 – 3071 = 1065 for NO PMRT 4204 – 2052 = 2152; ˆn: The number of patients corresponds to the percentage for each survival outcome (calculated by multiplying the % with the total number of patients for each study)

Table 2. Subgroup analysis for stage 1-2. Pooled analysis for studies that included stage 1-2

	Author (year)	cN+ rendered ypN0 post NAC patients *n* =	Stage	ypN0 PMRT+(RNI) patients *n* = LRRFS/DFS/OS (%) patients *n*^ =	ypN0 NO PMRT patients *n* = LRRFS/DFS/OS (%) patients *n*^ =
Retrospective	Dai et al. (16) (2023)	116	1-2	31 -/90.2/96.7 *n* = 0/28/30 (5 year)	85 -/93.7/97.3 *n* = 0/80/83 (5 year)
Retrospective	Wang et al. (17) (2020)	142	1-2	110 94.5/88.7/96.1 *n* = 104/98/106 (5 year)	32 90.1/72.4/95.0 *n* = 29/23/30 (5 year)
Retrospective	Muhsen et al. (19) (2018)	1087	1-2	163 (150) 96/75/81 *n* = 156/122/132 (10 year)	924 93/73/80 *n* = 859/675/739 (10 year)
Retrospective	Zeidan et al. (20) (2018)	684	1-2	337 97.5/77.3/81.7 *n* = 329/261/275 (10 year)	347 93.5/75.9/78.3 *n* = 324/263/272 (10 year)
Retrospective	Kim et al. (21) (2017)	714	1-2	130 (All) 97/94/98 *n* = 126/122/127 (5 year)	584 96/90/96 *n* = 561/526/561 (5 year)
Total		2743		771 *n* = 715*/631/670 % (96.6/81.8/86.9	1972 *n* = 1773*/1567/1685 % (94.0/79.5/85.4)

PMRT: Post-mastectomy radiotherapy; LRRFS: Locoregional recurrence-free survival; DFS: Disease-free survival; OS: Overall survival; NAC: Neoadjuvant chemotherapy; *: Number of patients for studies with no LRRFS were deducted for PMRT 771 = 740 and for NO PMRT 1972 - 85 = 1887; ^: The number of patients corresponds to the percentage for each survival outcome (calculated by multiplying the % with the total number of patients for each study)

The primary 5-year results of the NSABP B-51 trial recently presented in the SABCS (Dec. 2023) shed light on the role of RNI (15). This prospective trial's protocol specified the final analysis would take place after 172 events, or 10 years after study initiation. It looked at the benefit of RNI on survival in patients who were cN+ and converted to ypN0 after NAC. The number of patients recruited for disease-related end points was 1556. Patients were randomly assigned, with half of them receiving CW irradiation plus RNI after mastectomy or WB irradiation plus RNI after BCS. The other half received no RNI, instead undergoing observation after mastectomy or WB irradiation after BCS. The 5-year estimated LRRFS result for the NO RNI *vs.* RNI was 98.4% *vs.* 99.3% (HR = 0.37; 95% CI, 0.12–1.16), for DFS was 88.5% *vs.* 88.3 (HR = 1.06; 95% CI, 0.79–1.44), and for OS was 94 *vs.* 93.6 (HR = 1.12; 95% CI, 0.75–1.68), respectively. They concluded that the addition of RNI to PMRT or WB did not improve survival outcomes when compared to NO RNI or NO PMRT. Follow-up of patients for long-term outcomes continues. In a retrospective study, Cho et al. (44) found that in patients who achieved ypN0 after NAC and BCS, RNI did not improve LRC or survival, regardless of the subtype or primary tumor response, which is in agreement with the aforementioned trial. In addition to NSABP B-51, the SUPREMO prospective trial, an international trial with most patients contributing from the UK, Europe, and countries such as China, Japan, and Canada, among others, specifically looks at radiotherapy benefits in patients who underwent mastectomy with 1-3 positive LNs. These trials will contribute to the basis of radiotherapy administration in this specific group of patients once the final results are published.

The current pooled analysis is limited by the retrospective nature of the studies included, which contributes to selection bias. Most of the studies are T1-2, which might have influenced the outcome. The analysis for T2-3 is limited by the small number of patients analyzed. However, the inclusion of T1-3 studies in this analysis encompasses the relevant T-stages.

PMRT does not seem to confer survival benefits on patients with T1-3 tumors and 1-3 positive LNs. However, a concrete statement cannot be made in this regard for stage T3 patients due to the small number of patients analyzed. Clinicopathological factors that influence LRR, such as age less than forty, LVI, and tumor size, have to be taken into account before patients can forgo PMRT. Prospective studies with long-term follow-up are required to confirm these findings. These studies also have to take into account the aforementioned prognostic factors. Furthermore, the role of PMRT in the different BC subtypes requires further assessment. The ongoing phase 3 clinical prospective trials' results are essential in guiding the de-escalation of radiotherapy.

Table 3. Pooled analysis for studies that included stage 2-3

	Author (year)	cN+ rendered ypN0 post NST patients *n*=	Stage	ypN0 PMRT+(RNI) patients *n*^ = LRRFS/DFS/OS (%) patients *n* =	ypN0 NO PMRT patients *n*^ = LRRFS/DFS/OS (%) patients *n* =
Retrospective	Liu et al. (24) (2016)	1560	2-3	903 -/-/84.6 *n* = 0/0/764 (5 year)	657 -/-/81.7 *n* = 0/0/537 (5 year)
Retrospective	Shim et al. (25) (2014)	151	2-3	105 (All) 98.1/91.2/93.3 *n* = 103/96/98 (5 year)	46 92.3/83.0/89.9 *n* = 42/38/41 (5 year)
Retrospective	Le Scodan et al. (26) (2012)	134	2-3	78 96.2/79.2/88.3 *n* = 75/62/69 (5 year)	56 92.5/85.2/94.3 *n* = 52/48/53 (5 year)
Total		1845		1086 178*/158#/931 % (97.3/86.3/85.7)	759 94*/86#/631 % (92.2/84.3/83.1)

PMRT: Post-mastectomy radiotherapy; LRRFS: Locoregional recurrence-free survival; DFS: Disease-free survival; OS: Overall survival; NAC: Neoadjuvant chemotherapy; *: Number of patients for studies with no LRRFS were deducted for PMRT 1086-903 = 183 and for NO PMRT 759 - 657 = 102; #: Number of patients for studies with no DFS were deducted for PMRT 1086 – 903 = 183 for PMRT NO PMRT 759 – 657 = 102; ^: The number of patients corresponds to the percentage for each survival outcome (calculated by multiplying the % with the total number of patients for each study)

Table 4. *P*-value for T1-2/ T2-3

Stage	LRRFS *p*-value	DFS *p*-value	OS *p*-value
T1-2	0.67	0.66	0.81
T2-3	0.83	0.97	0.69

LRRFS: Locoregional recurrence-free survival; DFS: Disease-free survival; OS: Overall survival

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