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ORIGINAL ARTICLE

Tumor response and patient outcome after preoperative radiotherapy in locally advanced non-inflammatory breast cancer patients

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Summary

Purpose: *The purpose of this analysis was to assess the tumor response and long-term outcome in patients treated with preoperative radiotherapy (PRT) without systemic therapy.*

Methods: *Between 1997 and 2000, 134 patients with non-inflammatory locally advanced breast cancer (LABC) were treated with PRT. The tumor dose was 45 Gy in 15 fractions to the breast and to regional lymph nodes over 6 weeks. Radical mastectomy was performed 6 weeks after PRT to all patients and adjuvant systemic therapy was administered as per protocol. The measures of disease outcome were overall survival (OS) and disease-free survival (DFS) which estimated using the Kaplan-Meier method.*

Results: *Median follow-up was 74 months (range 4-216). Objective clinical tumor response after PRT was observed in 77.6% of the patients. Clinical complete tumor response (cCR) was achieved in 21.6% of the patients. Pathological CR in the breast was achieved in 15% of the patients. The 5- and 10-year OS were 55.1 and 37.8%, respectively. The 5- and 10-year DFS were 39.2 and 27%, respectively. Patients who achieved cCR had significantly longer OS in comparison with patients achieving clinical partial response (cPR) and clinical stable disease (cSD). Similarly, DFS of patients in the cCR group was longer compared with patients with cPR and cSD, yet without statistical significance.*

Conclusions: *Our results showed that local control in LABC patients achieved by primary PRT, followed by radical mastectomy was comparable with the results reported in the literature. Complete pathologic response to PRT identified a subgroup of patients with a trend toward better DFS and OS.*

Key words: *locally advanced breast cancer, preoperative radiotherapy, response to neoadjuvant therapy*

Introduction

Radiation therapy (RT) has a very important role in the multidisciplinary treatment of different stages of breast cancer. RT has been clearly demonstrated to reduce locoregional and distant relapse after breast conserving surgery (BCS) and after radical mastectomy. Moreover, overviews by the Early Breast Cancer Trialists Collaborative Group (EBCTCG) demonstrates, for the first time, that postoperative RT is not only important in achieving locoregional control, but also has significant influence on long-term survival [1-3]. Whole breast RT after BCS reduces the 10-year risk of any first recurrence (including locoregional and distant) by 15% and the 15-year risk of breast cancer-related mortality by 4% [2]. Post-mastectomy RT in node-positive patients reduces the 10-year risk of recurrence by 10% and the 20-year risk of breast cancer-related mortality by 8% [3].

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Patients presenting with LABC belong to a heterogeneous group of patients with different disease outcomes regarding locoregional and distant recurrence rates and survival. According to TNM staging this group includes patients with large primary tumor, greater than 5 cm (T3) or with skin/chest wall involvement (T4), and/or fixed axillary (N2) or supraclaviculary lymph nodes (N3), meaning IIIA to IIIC disease stages [4-6]. The majority of patients with LABC presents with an unresectable tumors and have poor prognosis and decreased survival.

Primary (neoadjuvant) chemotherapy (PCT) followed by local therapy, surgery or RT or both, has become the standard of care for patients with LABC [7-11]. PRT today is indicated after PCT if tumor resectability was not achieved [12,13]. However, before the introduction of PCT in the therapeutic strategy, PRT was more frequently used as the sole neoadjuvant approach for initially inoperable tumors, in order to reduce tumor volume and create a field permitting radical surgery [14-17]. PRT combined with mastectomy improved local and regional control rates, but did not modify survival rates. Moreover, in light of the deficient PRT's literature data, the treatment results are inconclusive regarding the full benefits of PRT.

Also, predictive factors for the response to RT are less frequently investigated compared to systemic therapy. The neo-adjuvant setting seems to be an ideal model for researching the predictive value of markers. In our previous analysis [18] a limited number of patients in stage III BC, treated only with PRT, we have found that 98 genes were significantly differentially expressed [False Discovery Rate (FDR) < 0.05] between PRT responders and non-responders.

The purpose of this analysis was to assess the tumor response and long-term outcome in patients treated with PRT alone, without systemic therapy**.**

Methods

Treatment

Between 1997 and 2000, 134 patients with non-inflammatory LABC (stage IIIA and IIIB) were treated with PRT at the Institute for Oncology and Radiology of Serbia**.** Radical mastectomy was performed 6 weeks after PRT to all patients and adjuvant systemic therapy was administered as per protocol.

The staging procedure included the following: clinical examination, mammography, chest X-ray, liver sonography, bone scans, complete blood count and serum biochemistry. After biopsy of the primary tumor and histologically proved breast cancer diagnosis, PRT was performed using Cobalt 60 (1,25-MV photons), or linear accelerator (6-MV photons). The tumor dose was 45 Gy in 15 fractions (3 Gy per fraction) every second day to the breast and to regional lymph nodes over 6 weeks. The whole breast was treated through medial and lateral tangential fields using wedges to correct for inhomogeneity. The dose was prescribed at a point in the midplane of the breast. Supraclavicular and axillary nodes were treated through anterior axillary-supraclavicular field with calculated doses at the 1/3 of the antero-posterior diameter. The internal mammary nodes were irradiated using a direct anterior filed, which covered ipsilateral nodes in the first 3 intercostal spaces. Doses were specified at a depth of 2-3 cm. Internal mammary nodes were treated with combination of photon beams (30 Gy) and electron beam (15 Gy) in order to decrease cardiac toxicity.

Six weeks after the completion of irradiation, radical mastectomy and axillary nodal dissection were performed to all patients. After mastectomy patients received 6 courses of chemotherapy consisting of cyclophosphamide, methotrexate and 5-fluorouracil (CMF) or 5-fluorouracil, doxorubicin and cyclophosphamide (FAC), and/or endocrine therapy (tamoxifen +/- castration by irradiation) as per protocol.

Clinical response to PRT in the breast was defined according to RECIST criteria [19]: complete response (cCR) if there was no palpable tumor in the breast; partial response (cPR) if regression of tumor was more than 30%; stable disease (cSD) if tumor regression was less than 30% or tumor progression less than 20% and progressive disease (cPD) if tumor progression was more than 20%. However, patients with cPD were not included in this analysis.

The definition of pathological complete remission (pCR) was as follows: pCRB if there was no invasive cancer in breast with/without ductal carcinoma *in situ* (DCIS) (yT0 or yTis) and with/without negative regional axillary lymph nodes (yN0 or yN1) and total pCR (tpCR) if there was pCRB associated with negative regional axillary lymph nodes (yT0 or Tis and yN0).

Hormone receptors determination

Histology, tumor size and grade, lymph nodes involvement and hormone receptors (HR) status were determined after the definitive surgery from formalin-fixed paraffin-embedded (FFPE) invasive breast cancer tissues. Hormone receptor contents were prospectively determined in tumor specimens by classical biochemical dextrane-coated charcoal (DCC) method in 81 patients after radical surgery [20]. The cut off values to discriminate between negative and positive HR status for estrogen receptor (ER) and progesterone receptor (PgR) were 10 fmol/mg protein and 20 fmol/mg protein, respectively.

Statistics

The primary endpoints of disease outcome were

Table 1. Patient, disease and treatment characteristics

Characteristics	*n (%)*
Number of patients	134 (100)
Age (years)	
Median (range)	52.5 (34-71)
Mean (SD)	53.4 (8.9)
≤ 50	59 (44.0)
> 50	75 (56.0)
Menopausal status	
Premenopausal	58 (43.3)
Postmenopausal	76 (56.7)
Clinical stage at diagnosis	
Stage III A	93 (69.4)
Stage III B	41 (30.6)
Clinical T stage	
T1	4 (3.0)
T2	67 (50.0)
T3	22 (16.4)
T4	41 (30.6)
Clinical N stage	
N0	3 (2.2)
N1	13 (9.7)
N2	118 (88.1)
Histology (biopsy)	
Ductal	56 (41.8)
Lobular	33 (24.6)
Other	45 (33.6)
Histologic grade	
Grade 1	1 (0.7)
Grade 2	86 (64.2)
Grade 3	6 (4.5)
Unknown	41 (30.6)
Nodal status (after mastectomy)	
Negative	23 (17.2)
Positive	111 (82.8)
Hormone receptor status	
ER-neg/PgR-neg	35 (26.1)
ER-pos and/or PgR-pos	46 (34.3)
Unknown	53 (39.6)
Adjuvant systemic therapy	
Yes	127 (94.8)
No	7 (5.2)
Kind of adjuvant chemotherapy	
CMF	57 (42.5)
FAC	46 (34.4)
No chemotherapy	31 (23.1)
Adjuvant endocrine therapy	
Tamoxifen	44 (32.8)
Castration by irradiation	8 (6.0)
Tamoxifen + castration by irradiation	3 (2.2)
No hormonal therapy	79 (59.0)

ER: oestrogen receptor, PgR: progesterone receptor, CMF: cyclophosphamide, methotrexate, 5-fluorouracil, FAC: 5-fluorouracil, doxorubicin, cyclophosphamide

OS, calculated from the time of tumor biopsy until the time of death from any cause, and DFS defined as the time from radical surgery until the time of the first locoregional and/or distant disease relapse, or death without disease relapse.

OS and DFS curves were estimated using the Kaplan-Meier method and univariate statistical analysis by log rank test was used to assess the difference in time to event (OS/DFS) between the analyzed groups.

Results

The median follow-up of 134 patients (median age 52.5 years, range 34-71) included in this study was 74 months (range 4-216). Patient characteristics are presented in Table 1.

An objective clinical tumor response after PRT was observed in 104/134 (77.6%) patients. cCR was achieved in 29/134 (21.6%) patients. Six weeks after finishing PRT, radical mastectomy was performed to all patients. tpCR in the breast was achieved in 20/134 (15%) patients and among them 10/134 (7.5%) had tpCR (Table 2).

HR status was determined in 81 patients and cCR was more frequently associated with patients with HR-negative than in patients with HR-positive tumors (25% vs 15.5%) but this difference was not statistically significant (Pearson chi-square test, p=0.33) (Table 3).

Adjuvant chemotherapy and/or endocrine therapy were administered after completion of locoregional therapy. Seventy-one out of 134 (52.9%) patients received chemotherapy: 40/134 (29.8%) patients received CMF and 31/134 (23.1%) received

Table 2. Tumor response to preoperative radiotherapy

Clinical response	*n (%)*	*Pathological response*	*n (%)*
cCR	29 (21.6)	pCRB	20 (15.0)
cPR	75 (56.0)	tpCR	10 (7.5)
cSD	30 (22.4)	non-tpCR	124 (92.5)
Total	134 (100)	Total	134 (100)

cCR: clinical complete response, cPR: clinical partial response, cSD: clinical stable disease, pCRB: in-breast pathology complete response, tpCR: total pCR

Table 3. Clinical tumor response to preoperative radiotherapy according HR status

Clinical response to PRT	*ER-neg/PgR-neg n (%)*	*ER-pos and/or PgR-pos n (%)*	*p value*
cCR	9 (25)	7 (15.5)	0.33
cPR	21 (58.3)	25 (55.6)	
cSD	6 (16.7)	13 (28.9)	
Total	36 (100)	45 (100)	

HR: hormone receptor, ER-neg: negative ER status of the primary, ER-pos: positive ER status of the primary, PgR-neg: negative PgR status of the primary, PgR-pos: positive PgR status of the primary, PRT: preoperative radiotherapy

Table 4. Sites of the first disease relapse

Sites of disease relapse	*n (%)*
Locoregional relapse	10 (7.5)
Isolated locoregional relapse	4 (3.0)
Locoregional relapse plus distant mets	6 (4.5)
Distant metastases	
Bones	24 (17.9)
Visceral	25 (18.6)
Soft tissues	7 (5.2)
Brain	3 (2.2)
Multiple distant sites	14 (10.5)

FAC, 24/134 (17.9%) adjuvant endocrine therapy (tamoxifen or castration by irradiation) and 32/134 (23.9%) patients received combination of chemotherapy and endocrine therapy.

At the time of analysis 83 patients (61.9%) developed disease relapse. The first relapse sites are presented on Table 4.

Eighty three out of 134 patients (61.9%) died: 67/134 (50%) from breast carcinoma and 16/134 (11.9%) from other causes. The 5- and 10-year OS were 55.1% (95% CI 47-64%) and 37.8% (95% CI 29-48%), respectively. The 5- and 10-year DFS

Table 5. OS and DFS according to clinical tumor response to PRT

Clinical response to PRT	*n*	*OS (mos) (95% CI)*	*p*	*DFS (mos) (95% CI)*	*p*
cCR	29	145 (>75)		110 (>36)	
cPR	75	65 (46-90)	0.038	31 (24-51)	NS
cSD	30	71 (34-171)		39 (20-78)	

OS: overall survival; DFS: disease-free survival, PRT: preoperative radiotherapy, n: number of patients, mos: months, 95%CI: 95% confidence interval, NS: non-significant

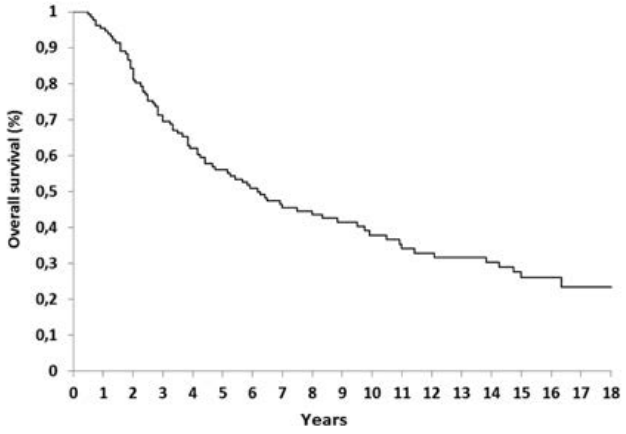

Figure 1. Overall survival, all patients.

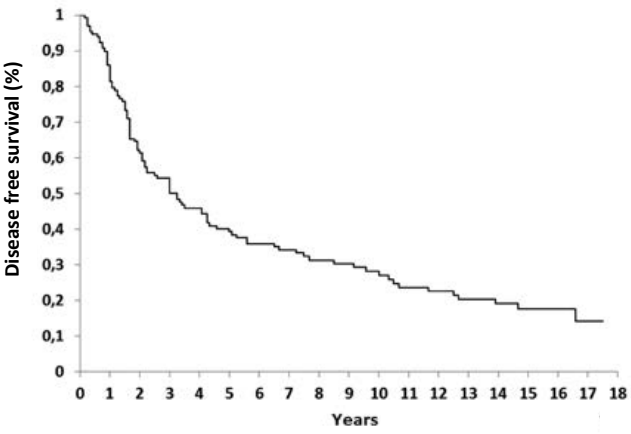

Figure 2. Disease - free survival, all patients.

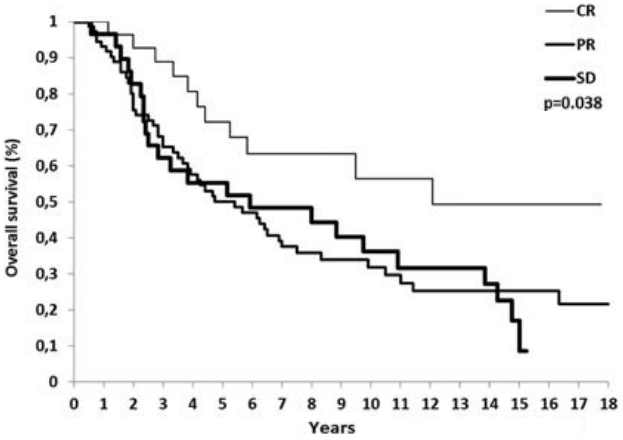

Figure 3. Overall survival according to clinical response to preoperative radiotherapy.

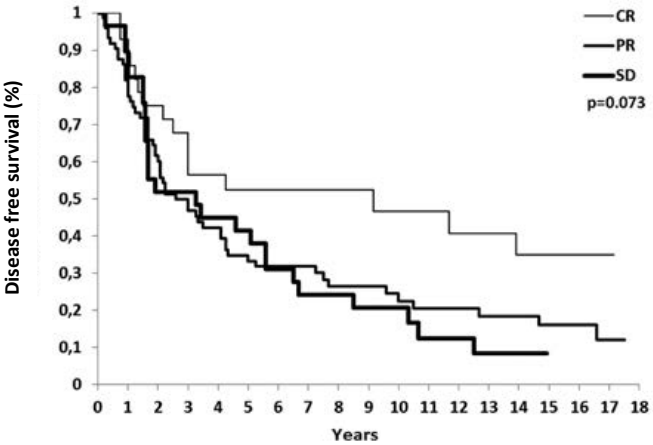

Figure 4. Disease-free survival according clinical response to preoperative radiotherapy.

Table 6. OS and DFS according to pathological response to PRT

Pathological response to PRT	*n*	*OS (mos) (95% CI)*	*p*	*DFS (mos)(95% CI)*	*p*
tpCR	10	145 (>114)	0.096	140 (>39)	0.056
non-pCR	124	70 (50-106)		36 (24-51)	

OS: overall survival, DFS: disease-free survival, PRT: preoperative radiotherapy, n: number of patients, mos: months, 95%CI: 95% confidence interval, NS: non-significant

were 39.2% (95% CI 31-48) and 27% (95% CI 19-36%), respectively. Median DFS and OS for the whole group was 39 months (95% CI 26-55) and 74 months (95% CI 53-117), respectively. These results are shown in Figures 1 and 2.

We also analyzed the disease outcome according to the tumor response to PRT. This analysis showed that patients who achieved cCR had significantly longer OS in comparison with patients achieving cPR and cSD (log-rank test, p=0.038) (Table 5, Figure 3). Similarly, DFS of patients in the cCR group was longer compared with patients with cPR and cSD, although this difference did not reach statistical significance (Table 5, Figure 4).

Ten-year OS and DFS in patients with different clinical tumor response to PRT were as follows: 56% and 46% in patients with cCR, 31% and 22% in patients with cPR and 36% and 16% in patients with cSD.

There was a trend toward longer DFS in patients achieving tpCR compared with patients with non-tpCR to PRT. However, although OS in patients achieving tpCR was longer compared to patients not achieving tpCR (145 vs 70 months), this difference did not reach statistical significance (Table 6).

Discussion

According to current recommendations the majority of patients with LABC are treated with the combination of PCT, surgery and RT [8,12, 13,21,22]. Generally, the goal of neoadjuvant therapy is to reduce tumor volume and achieve resectability to allow for radical surgery. PCT usually consists of 6-8 cycles of a combination of anthracyclines and taxanes and human epidermal growth factor receptor 2 (HER2)-targeted therapy in case of HER2 positive BC. However, the indication for PCT has been extended in large operable tumors in order to enable less extensive surgery. An update analysis of the first two clinical trials (NSABP-B-18 and B-27) designed to compare the efficacy of PCT and adjuvant CT in patients with large operable tumors showed that preoperative therapy is equivalent to adjuvant therapy [23]. The role of PRT in this context would be in further tumor shrinkage in case of PCT failure to achieve resectability.

For decades before the introduction of PCT, PRT was usually used as sole preoperative treatment for patients presenting with LABC. In the recent literature there is little information on the implementation of PRT as single initial therapy in the treatment of LABC. Only few articles have reported results of PRT before radical mastectomy and conservative surgery in the last few years. Santos et al. published results of PRT for 203 LABC patients after 26 years of follow-up [24]. PRT was performed with tumor dose 45 Gy in 25 fractions to the breast, ipsilateral axillary, supraclavicular and internal mammary lymph nodes. After finishing PRT all patients had radical mastectomy. Pathological CR in the breast was observed in 16% of patients and 10- and 20-year local control rates were 90% and 84%, respectively. The 10- and 20-year DFS rates were 49% and 35%, and the 10- and 20-year OS rates were 56% and 41%, respectively. Patients with pCR tended to have better DFS (log-rank test, p=0.06) and OS (log-rank test, p=0.07) when compared to patients with PR or SD.

Another report of PRT followed by conservative surgery for T2 and T3 BC patients was presented by Calitchi E et al. [25]. Seventy five patients were treated initially with RT (45 Gy in 25 fractions to the breast and regional lymph nodes). After tumorectomy a postoperative boost to tumor bed of 20 Gy using iridium-192 was performed. Adjuvant chemotherapy and/or endocrine therapy were administered after completion of locoregional treatment. In-breast pCR rate was noted in 11% of the patients. After median follow-up of 10 years, 47% of the patients developed disease relapse, and locoregional relapse rate was noted in 12% of the treated patients.

In our group of 134 LABC patients, the pCR rate in the breast after PRT was similar (15%) compared to the reports in the literature (11–16%). Relapse of disease was observed in 61.9% of our patients, while 7.5% had locoregional relapse. The 5-and 10-year OS was 55% and 37.8% respectively, and 5- and 10-year DFS was 39.2% and 27%, respectively. Our results of the local control

rate are quite similar to both reported studies (10-year local control rate about 90%). However, the relapse rate was somewhat higher, while 10-year OS rate was lower in our patients comparing to other reported studies. The possible reason for this might be the difference in adjuvant systemic therapy received after definitive locoregional therapy. Also, 88% of the patients in our study had initial clinical N2 status, while after mastectomy 83% had pN-positive disease, which could be another reason for lower OS and DFS compared to reported data. Santos et al. reported that initially 56% of the patients had palpable axillary lymph nodes, while 31% were classified as pN0 after PRT and mastectomy [24]. In the report of Calitchi et al. [25], among 75 analyzed patients only one had clinical N2 status. Others were classified as cN0 (75%) and cN1 (14%). Hence, most of our patients had advanced axillary nodal disease (N2) with expected poor survival. Concerning the association of pCR and disease outcome, we noticed that patients who achieved pCR to PRT had significantly better disease outcome.

There are several pathologic response classification systems after PCT [26,27] but highly accepted criterion for the definition of pCR includes no invasive tumor in the breast (yT0) and no involved regional axillary lymph nodes (yN0). Patients achieving pCR following anthracycline-based PCT experience significantly superior DFS and OS compared with non-responders [23]. pCR rates following standard multi-agent CT remain relatively low, ranging from 7-31% [28,29] with the exception of patients with HER2-positive BCs that achieved pCR rates up to 50% when treated with HER2 targeted therapy such as trastuzumab and lapatinib [30,31] or trastuzumab and pertuzumab [32,33].

The achievement of pCR (including residual DCIS in breast) to PCT is a surrogate marker of better disease outcome in patents with triple negative BCs or HER2 positive BCs, especially in HR-negative/HER2-positive BC patients [34]. The first investigated predictive factor regarding response to PCT was HR status. It was shown that patients with invasive lobular carcinoma, the majority of whom were HR-positive, had the lowest response rate but with no influences on disease outcome [35].

The predictive value of the primary tumor HR status for the response to PRT is not precisely established. In our analysis tumor HR status did not influence the clinical response to PRT although non-significantly higher response rate was noticed in patients with HR-negative compared to HR-positive BCs (25 and 15%, respectively). Similarly, only 8/10 patients achieving tpCR had their HR status determined, and majority of them (5/8 patients) had HR-negative status of the primary tumor (data not shown). We did not divide patients into various biology BC subtypes groups because of the low number of patients.

In our previously reported analysis [18] we identified a set of 98 genes significantly differentially expressed (false discovery rate/FDH; $p<0.05$) between responders and non-responders to PRT. Ingenuity Pathway Analysis was used to determine molecular functions significantly associated with this gene list and included regulation of cellular growth and proliferation, cell cycle, cell death and survival as top scoring function. Canonical pathways for G2/M DNA damage checkpoint regulation and GADD45 genotoxic stress signaling were significantly enriched (FDR<0.05) among differentially expressed gene list between RT resistant and RT sensitive tumors. However this analysis was done on 18 patients only (10 responders and 8 non-responders).

Since patients who achieved cCR after PRT had better DFS and OS rates compared with patients with non-cCR, it seems that the achievement of pCR to PRT might be a surrogate marker of better disease outcome in these patients. Also, longer OS and DFS in patients achieving cCR compared to patients with no cCR in our analysis are in line with the previous observations [9,22,34].

Another developed strategy in the treatment of LABC is concurrent administration of PCT and PRT. Semiglazov et al. conducted a randomized phase III trial comparing concomitant PCT/PRT with PRT alone in 271 LABC (stage IIB-IIIA) patients [36]. PCT consisted of thiotepa, methotrexate and 5-fluorouracil, while PRT was performed to the breast with a total dose of 60 Gy /2 Gy per fraction, and 40 Gy to the regional lymph nodes. In-tumor pCR was found in 29.1% of the patients in the combined group vs 19.4% in PRT alone group ($p<0.05$). The estimated 5-year OS rates in the combined vs PRT alone groups were 86.1 and 78.3% respectively (log rank test, $p>0.05$) and 5-year DFS rates were 81 vs 71.6%, respectively (log rank test, $p<0.05$).

Shanta et al. in their early report [37] also compared concurrent PCT/PRT (CMF combined with irradiation of the breast and regional lymph nodes with dose of 40 Gy in 20 fractions) with PRT only. Complete tumor remission in the breast was achieved in 42.1% in the PCT/PRT group vs 18.9%

in the PRT group. The authors noticed significant survival advantage in the combined PCT/PRT group. The 5-year DFS was 60.6% in the PCT/PRT group vs 47.5% in the PRT alone group (p<0.005). The largest report on PCT/PRT combination was published also by Shanta et al. [38] who retrospectively analyzed a group of 1117 patients with LABC treated concomitantly with PCT consisting of CMF or FAC, or 5-fluorouracil, epirubicin and cyclophosohamide (FEC) and PRT with tumor dose 40 Gy in 20 fractions to the breast and regional lymph nodes. The pCR rate was 45.1%, with a low locoregional relapse rate of 7%. The OS rate at 5 and 10 years was 75.6 and 63.9% respectively, and the corresponding rate for DFS was 64.5 and 52.6%, respectively. The best survival rate was seen among patients achieving pCR. The authors reported minimal toxicities of concurrent PCT/PRT. Interruption of RT was minimal (less than 5% of patients), while skin morbidity usually consisted of mild to severe dry desquamation and hyperpigmentation.

The next report of concurrent PCT/PRT was published by Alvarado-Miranda et al. [39] who treated 112 LABC patients (stage IIB-IIIB). PCT consisted of FAC or AC (doxorubicin, cyclophosphamide) followed by concomitant CT/RT (weekly mitomycin, 5-FU and dexamethasone or cisplatin, gemcitabine and dexamethasone combined with irradiation of the breast and regional lymph nodes with tumor dose 50 Gy in 5 weeks and boost to the residual disease with 10 Gy). The authors reported in-breast pCR of 42%, while after mean follow-up of 43 months the 5-year DFS and OS rate were 76.9 and 84.2%, respectively. Only one patient had local recurrence. The most frequent adverse events were grade 1-2 neutropenia in 32.2% and grade 3 radio-epithelitis in 22.4% of the patients.

The concomitant paclitaxel and PRT efficacy in 105 LABC patients was also investigated by Adams et al. [40]. Paclitaxel was administered for 10-12 weeks with PRT with a total dose 45 Gy (1.8 Gy per fraction) to the breast and axillary and supraclavicular lymph nodes, with a boost of 14 Gy (2 Gy per fraction**)** on the tumor. pCR and pPR after PCT/PRT was achieved in 34% of the patients and associated with significantly better DFS and OS. The median follow-up was 60 months and the estimated 5-year DFS and OS rate were 61.4 and 71.6%, respectively.

Alvarado-Miranda et al. [39] considered also the impact of ER expression on pCR rate after neoadjuvant treatment. They reported that patients with ER-negative BCs were significantly more likely to achieve pCR during PCT/PRT compared to patients with ER positive-tumors. These findings are similar to the results reported by Adams et al. [40]. They found pCR rate of 54% in patients with ER-negative BCs vs 18% in patients with ER-positive tumors (log rank test, p<0.0001). In our group of patients HR content was determined in 81/134 (60%) patients. Tumor pCR was more frequently achieved in patients with HR-negative vs HR-positive BCs, but this difference was not statistically significant.

According to presented latest literature data, pCR rate in LABC patients is more than 2-fold higher in patients treated with combined PCT/PRT than with PRT alone. OS and DFS rates are also higher in patients treated with PCT/PRT combination than PRT alone as well.

Conclusion

Our results showed that local control in LABC patients achieved by PRT followed by radical mastectomy was comparable with the results reported in the literature. pCR to PRT identified a subgroup of patents with a trend toward better DFS and OS. Further investigation based on biological markers between responders and non-responders to PRT are needed to establish the optimal multidisciplinary approach and the role of PRT in the combined treatment modality for LABC. According to literature the combined PCT/PRT strategy might be suitable for patients with inoperable LABC. and a successful treatment option.

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Conflict of interests

The authors declare no confict of interests.

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