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A population-based propensity score matching analysis of neoadjuvant compared to adjuvant chemotherapy in luminal breast cancer

Chenhui Zheng, Danni Zheng, Yuzhu Zhang, Renzhi Lin & Zhibao Zheng✉

This study evaluated the long-term prognosis of patients with luminal (HR+/HER2−) breast cancer who underwent either neoadjuvant or adjuvant chemotherapy. Between January 2014 and December 2018, 1065 h+/HER2− breast cancer patients were retrospectively analyzed. Each patient receiving neoadjuvant chemotherapy was matched with two patients receiving adjuvant chemotherapy using a 1:2 propensity score matching (PSM) approach. After matching, 47 neoadjuvant chemotherapy patients and 89 adjuvant chemotherapy patients were included. The clinical and pathological characteristics of both groups were compared, and risk factors for postoperative events were assessed alongside a survival analysis. Following propensity score matching, the characteristics of the two groups were well balanced. The study identified lower progesterone receptor (PR) expression, histological grade III, and lymph node metastasis as independent risk factors for recurrence-free survival (RFS). No significant difference in RFS was observed between neoadjuvant and adjuvant chemotherapy. It is recommended that patients with HR+/HER2− breast cancer who exhibit a poor response to neoadjuvant chemotherapy should undergo early surgery, with personalized treatment decisions based on postoperative pathological findings.

Keywords Breast cancer, Neoadjuvant chemotherapy, HR+/HER2−, Propensity score matching, Recurrence-free survival

Breast cancer is a significant global health issue, with HR+/HER2− subtypes representing approximately 70% of all invasive breast cancers[1]. Compared to other subtypes, HR+/HER2− is associated with a better prognosis, as most adverse events occur later, with peak periods of recurrence and metastasis typically appearing 5 to 10 years post-surgery[2]. Neoadjuvant chemotherapy(NACT) offers several advantages, including downstaging the disease preoperatively, reducing the extent of surgery, providing in vivo drug sensitivity data, and improving overall prognosis. It has been widely applied in breast cancer treatment, particularly for HER2-positive and triple-negative breast cancers, where it shows the best efficacy. However, HR+/HER2− subtype are relatively less responsive to chemotherapy[3], leading to less frequent use of both adjuvant and neoadjuvant chemotherapy in this subtype. Understanding the nuances between these approaches is vital for optimizing treatment efficacy while minimizing unnecessary toxicity.

Achieving pathologic complete response (PCR) following NACT is closely linked to significant improvements in RFS and overall survival[4]. However, HR+/HER2− patients tend to have reduced chemotherapy sensitivity and lower PCR rates[1,5]. The motivation for this research stems from the need to better stratify HR+/HER2− patients who may benefit from chemotherapy and determine the most appropriate timing of systemic therapy. Consequently, determining whether HR+/HER2− breast cancer patients who undergo NACT achieve better prognoses than those receiving adjuvant chemotherapy(ACT) remains a critical challenge in clinical decision-making[6]. Furthermore, patients receiving NACT often exhibit poorer clinical and pathological profiles compared to those undergoing ACT, introducing substantial bias between these two groups[7,8]. To address this, the study utilizes propensity score matching to align the baseline characteristics of both patient groups, thereby enabling a valid comparison of RFS between HR+/HER2− breast cancer patients treated with NACT versus ACT.

Department of Surgical Oncology, Taizhou Central Hospital (Taizhou University Hospital), Taizhou, Zhejiang, China. ✉email: zhengzb@tzc.edu.cn

This study is guided by the hypothesis that NACT may offer certain advantages over ACT in HR+/HER2− breast cancer, particularly in terms of facilitating breast-conserving surgery. However, it is hypothesized that the overall survival benefit may be equivalent between the two approaches, given the relatively modest chemosensitivity of this subtype. By exploring these hypotheses, this research seeks to contribute valuable data that may inform future clinical decision-making.

Methods

Patients

This retrospective study was approved by the institutional review board of our institution, with a waiver granted for the requirement of written informed consent. Data collection adhered to the relevant guidelines and regulations set forth by the committee and was conducted at a single center.

Patients with HR+/HER2− breast cancer, diagnosed between January 2014 and December 2018 at Taizhou Central Hospital, and clinically staged as T1-3N0-3M0, were selected based on inclusion criteria. The exclusion criteria were as follows: (1) male patients, (2) ductal carcinoma in situ (DCIS), (3) missing clinical or pathological data, (4) concurrent malignancies in other locations, and (5) incomplete neoadjuvant chemotherapy.After propensity score matching, 47 cases of neoadjuvant chemotherapy and 89 cases of adjuvant chemotherapy were included in the final analysis.

This retrospective study was approved by the institutional review board of (Institutional Ethics Committee of Taizhou Central Hospital) and due to the retrospective study was waiver granted by the institutional review board of (Institutional Ethics Committee of Taizhou Central Hospital) for the requirement of written informed consent(No.2024 L-07-58).

Study population and variables

The cohort characteristics include demographic features (age at diagnosis, menopausal status), clinical-pathological features (tumor size, N stage, histological type, histological grade, ER expression level, PR expression level, CerbB-2 expression level, Ki-67 proliferative index), treatment methods (breast surgery type, axillary surgery type, chemotherapy drugs), and survival status.

Interpretation of intrinsic subtype

The status of estrogen receptor (ER), PR, HER2, and Ki-67 levels was determined according to the guidelines of the College of American Pathologists (CAP)[9,10]. Hormone receptor positivity (HR+) was defined as ≥ 1% positive nuclear staining for ER and/or PR, confirmed by immunohistochemical (IHC) staining. HER2 staining was classified as negative for 0 and 1+, equivocal for 2+, and positive for 3+. In cases where IHC results were equivocal, fluorescence in situ hybridization (FISH) was used to confirm HER2 status. Menopausal status was assessed using the following criteria: (i) a history of bilateral oophorectomy, (ii) age > 60 years, (iii) age < 60 years with at least 12 months of amenorrhea (without chemotherapy, tamoxifen, toremifene, or ovarian suppression), and FISH and estradiol levels in the postmenopausal range, and (iv) for those on tamoxifen or toremifene, age < 60 years with FSH and plasma estradiol levels within the postmenopausal range.

Clinical outcome

RFS was defined as the time that elapsed from surgery to the first event of any breast cancer recurrence (local or distant) or death, according to the standardized definitions for efficacy end points (STEEP) criteria[11].

Statistical analysis

Statistical analysis and image generation were conducted using IBM SPSS version 26 (SPSS, Inc., Chicago, IL, USA) and R version 4.4.1. A two-sided *P*-value of < 0.05 was considered statistically significant. The chi-square test (χ^2) was employed to compare categorical variables between groups. Kaplan-Meier analysis and Cox regression were used to assess RFS. The effects of various prognostic factors on RFS, as well as the interaction between chemotherapy benefits and these factors, were evaluated using the Cox proportional hazards model. PSM was performed using R to address differences in clinicopathological characteristics and surgical approaches between the two groups. A 1:2 matching ratio was applied to balance confounding factors, with a caliper set at 0.05. RFS was analyzed both before and after matching.

Results

Clinicopathological characteristics

A total of 1354 patients were reviewed and 1065 eligible patients (78.7%) were included (Fig. 1). NACT was offered to 64 patients (6.4%), and those who underwent ACT accounted for 1001 patients (93.6%). According to the 8th edition of AJCC breast cancer staging, the NACT group had 5 cases of cT1, 47 cases of cT2, and 12 cases of T3, accounting for 7.8%, 73.4%, and 18.8%, respectively. In the ACT group, there were 597 cases of T1, 384 cases of T2, and 20 cases of T3, representing 59.6%, 38.4%, and 2.0%, respectively. Patients who received NACT tended to have larger tumors, with T2 and T3 stages making up 92.2%, compared to 40.4% in the ACT group. In the NACT group, 20 cases were cN0, 23 cases were cN1, and 21 cases were cN2-3, comprising 31.3%, 35.9%, and 32.8%, respectively. Meanwhile, in the ACT group, 843 cases were cN0, 111 cases were cN1, and 47 cases were cN2-3, corresponding to 84.2%, 11.1%, and 4.7%, respectively.In the NACT group, 57 patients (89.1%) underwent mastectomy, compared to 668 patients (66.7%) in the ACT group, showing a statistically significant difference ($P < 0.001$). Only 1 patient (1.6%) in the NACT group opted for sentinel lymph node biopsy, compared to 516 patients (51.5%) in the ACT group, with significant differences in axillary surgery methods ($P < 0.001$). Regarding chemotherapy regimens, in the NACT group, 2 patients (3.1%) received anthracycline-based

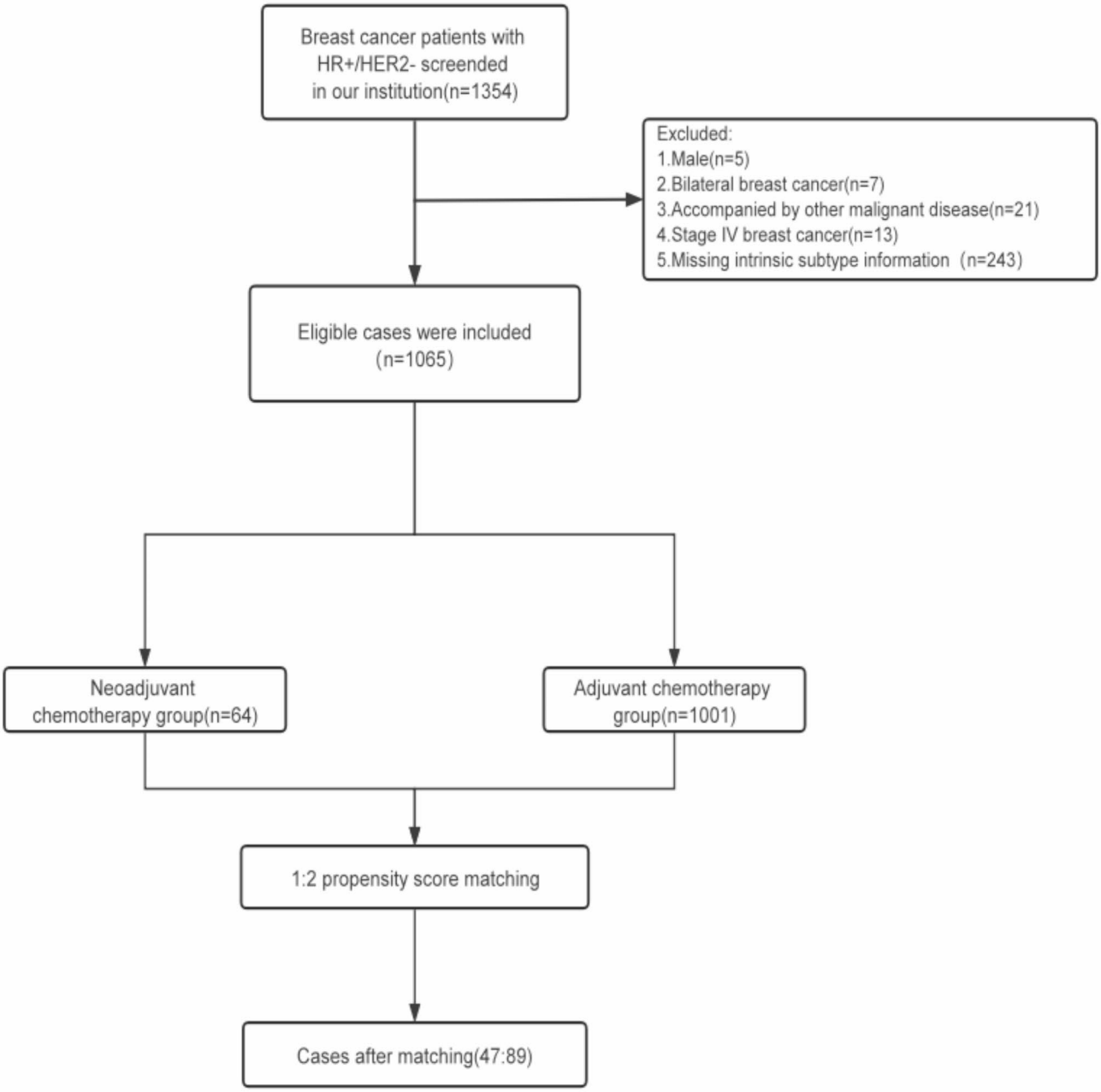

Fig. 1. Flow chart of study cohort selection.

regimens without taxanes, no patients received taxane-only regimens, 61 patients (95.3%) received anthracycline combined with taxanes, and 1 patient (1.6%) received other regimens. In the ACT group, 91 patients (9.1%) received anthracycline-based regimens without taxanes, 463 patients (46.3%) received taxane-only regimens, 434 patients (43.4%) received anthracycline combined with taxanes, and 13 patients (1.3%) received other regimens. A higher proportion of patients in the NACT group received more aggressive treatment regimens, with a statistically significant difference ($P < 0.001$) (Table 1).

Further, 1:2 PS matching resulted in 136 matched pairs. The NACT and ACT groups consisted of 47 and 89 patients, respectively, all baseline variables were well balanced between the two groups (Table 2). The propensity score distribution of patients in both groups became more aligned (Fig. 2). The median follow-up time for the PSM cohort was 67 months (interquartile range: 55–95 months), with a total of 23 recurrence recorded during the follow-up period.

Univariate and multivariate analysis of risk factors for postoperative complications

Univariate and multivariate logistic regression analyses were performed to identify risk factors for RFS. In univariate analysis, clinical nodal status(cN0 vs. cN1, HR 0.817, 95% CI 0.039–0.966, $P = 0.045$), grade (I–II vs. III, HR 0.936, 95% CI 0.007–0.262, $P = 0.001$) and PR (< 20% vs. ≥ 20%, HR 0.540, 95% CI 1.744–14.486,

Characteristics	NACT ($n = 64$)	ACT ($n = 1001$)	P
Age (years), no. (%)			0.145
≤ 35	7(10.9%)	63(6.3%)	
36–64	51(79.7%)	774(77.3%)	
≥ 65	6(9.4%)	164(16.4%)	
Menopausal status, no. (%)			0.126
Pre/peri-menopausal	35(54.7%)	449(44.9%)	
Post-menopausal	29(45.3%)	552(55.1%)	
Surgery of the breast, no. (%)			**< 0.001**
Breast-conserving surgery	7(10.9%)	333(33.3%)	
Mastectomy	57(89.1%)	668(66.7%)	
Surgery of the axilla, no. (%)			**< 0.001**
SLNB alone	1(1.6%)	516(51.5%)	
ALND	63(98.6%)	485(48.5%)	
Clinical tumor size, no. (%)			**< 0.001**
T1	5(7.8%)	597(59.6%)	
T2	47(73.4%)	384(38.4%)	
T3	12(18.8%)	20(2.0%)	
Clinical nodal status, no. (%)			**< 0.001**
N0	20(31.3%)	843(84.2%)	
N1	23(35.9%)	111(11.1%)	
N2–3	21(32.8%)	47(4.7%)	
Histologic subtype, no. (%)			0.102
IDC	58(90.6%)	959(95.8%)	
ILC	4(6.3%)	33(3.3%)	
Other HST	2(3.1%)	9(0.9%)	
Grade, no. (%)			**0.012**
I–II	33(51.6%)	589(58.8%)	
III	19(29.7%)	332(33.2%)	
UNKNOW	12(18.8%)	80(8.0%)	
ER, no. (%)			0.838
< 10	2(3.1%)	27(2.7%)	
≥ 10	64(96.9%)	974(97.3%)	
PR, no. (%)			0.987
< 20	25(39.1%)	390(39.0%)	
≥ 20	39(60.9%)	611(61.0%)	
CerbB-2, no. (%)			0.860
–	9(14.1%)	133(13.3%)	
1+/2+	55(85.9%)	868(86.7%)	
Ki67, no. (%)			0.912
< 30	36(56.3%)	556(55.5%)	
≥ 30	28(43.8%)	445(44.5%)	
Chemotherapy drugs, no. (%)			**< 0.001**
Anthracycline	2(3.1%)	91(9.1%)	
Taxanes	0(0.0%)	463(46.3%)	
Taxanes versus anthracycline	61(95.3%)	434(43.4%)	
Others	1(1.6%)	13(1.3%)	

Table 1. Clinicopathological characteristics of neoadjuvant chemotherapy group and non-neoadjuvant chemotherapy group. *NACT* neoadjuvant chemotherapy, *ACT* adjuvant chemotherapy, *SLNB* sentinel lymph node biopsy, *ALND* axillary lymph node dissection, *ER* estrogen receptor, *PR* progesterone receptor, *IDC* invasive ductal carcinoma, *ILC* invasive lobular carcinoma, *HST* histological special type. Significant values are in (bold).

$P = 0.003$) expression were significantly associated with RFS (Table 3). Subgroup analyses based on age($P > 0.007$) and tumor size($P > 0.007$) showed no significant differences in treatment effects across different age groups or tumor size subgroups. In multivariate analysis, clinical nodal statuss(cN0 vs. cN1, HR 0.658, 95% CI 0.046–0.612, $P = 0.007$), grade (I–II vs. III, HR 0.683, 95% CI 0.016–0.237, $P \leq 0.001$) and PR (<20% vs. ≥20%, HR

Characteristics	NACT (*n*=47)	ACT (*n*=89)	*P*
Age (years), No. (%)			0.687
≤ 35	2(4.3%)	4(4.5%)	
36-64	41(87.2%)	73(82.0%)	
≥ 65	4(8.5%)	12(13.5%)	
Menopausal status, No. (%)			0.579
Pre/peri-menopausal	24(51.1%)	41(46.1%)	
Post-menopausal	23(48.9%)	48(53.9%)	
Surgery of the breast, No. (%)			0.857
Breast-conserving surgery	3(6.4%)	5(5.6%)	
Mastectomy	44(93.6%)	84(94.4%)	
Surgery of the axilla, No. (%)			0.964
SLNB alone	1(2.1%)	2(2.2%)	
ALND	46(97.9%)	87(97.8%)	
Clinical tumor size, No. (%)			0.846
T1	5(10.6%)	12(13.5%)	
T2	38(80.9%)	71(79.8%)	
T3	4(8.5%)	6(6.7%)	
Clinical nodal status, No. (%)			0.985
N0	19(40.4%)	35(39.3%)	
N1	18(35.2%)	34(38.2%)	
N2–3	10(21.3%)	20(22.5%)	
Histologic subtype, No. (%)			0.635
IDC	44(93.6%)	85(95.5%)	
ILC	3(6.4%)	4(4.5%)	
Grade, No. (%)			0.175
I–II	24(51.1%)	43(48.3%)	
III	15(31.9%)	39(43.8%)	
UNKNOW	8(17.0%)	7(7.9%)	
ER, No. (%)			0.683
< 10	1(2.1%)	3(3.4%)	
≥ 10	46(97.9%)	86(96.6%)	
PR, No. (%)			0.816
< 20	17(36.2%)	34(38.2%)	
≥ 20	30(63.8%)	55(61.8%)	
CerbB-2, No. (%)			0.768
–	6(12.8%)	13(14.6%)	
1+/2+	41(87.2%)	76(85.4%)	
Ki67, No. (%)			0.857
< 30	24(51.1%)	44(49.4%)	
≥ 30	23(48.9%)	45(50.6%)	
Chemotherapy drugs, No. (%)			0.133
Anthracycline	2(4.3%)	0(0.0%)	
Taxanes	0(0.0%)	3(3.4%)	
Taxanes versus anthracycline	61(93.6%)	85(95.5%)	
Others	1(2.1%)	1(1.1%)	

Table 2. Clinicopathological characteristics of neoadjuvant chemotherapy group and non-neoadjuvant chemotherapy group after propensity score matching including sensitivity analyses. *NACT* neoadjuvant chemotherapy, *ACT*, adjuvant chemotherapy, *SLNB* sentinel lymph node biopsy, *ALND* axillary lymph node dissection, *ER* estrogen receptor, *PR* progesterone receptor, *IDC* invasive ductal carcinoma, *ILC* invasive lobular carcinoma, *HST* histological special type.

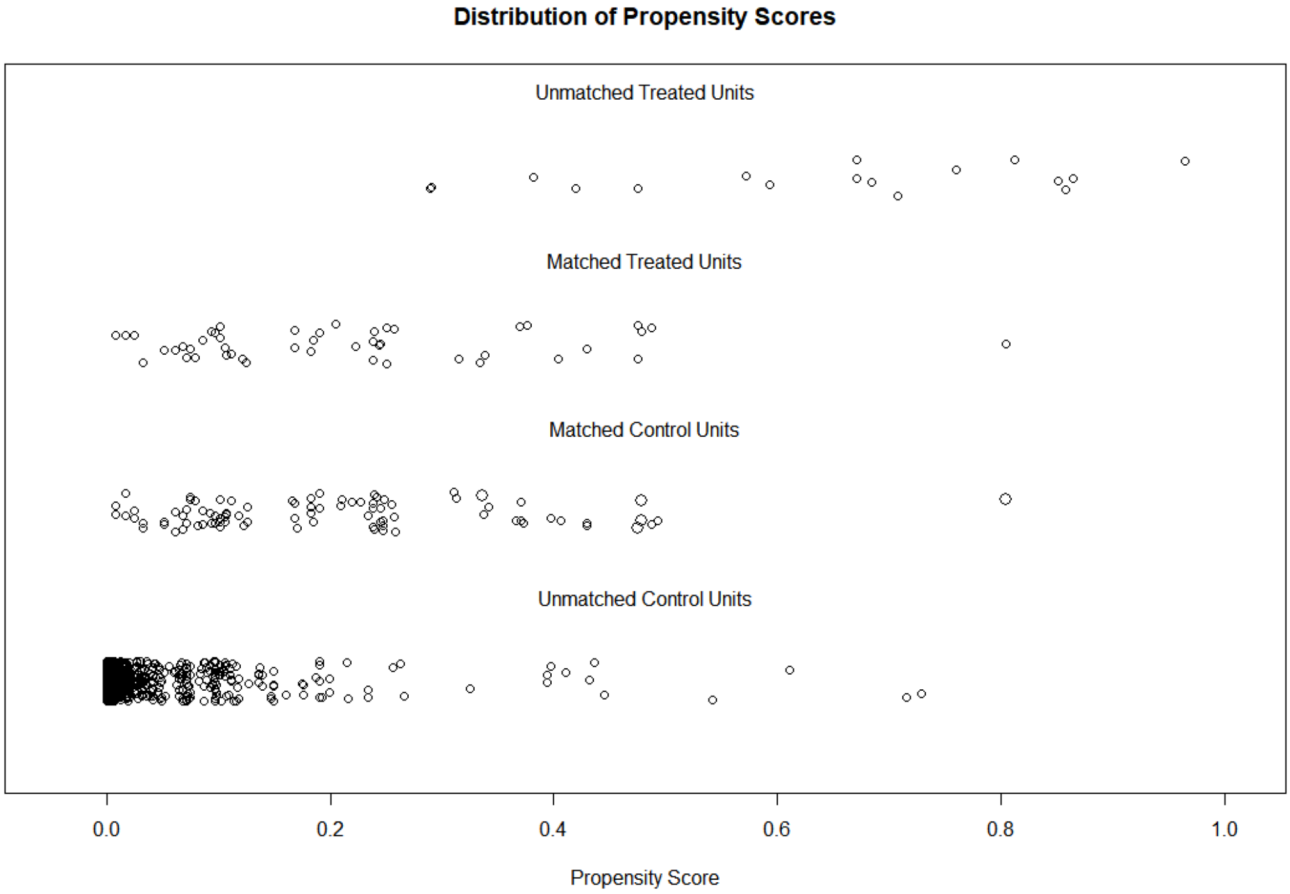

Fig. 2. PS Scatter p lot before and after matching.

0.485, 95% CI 1.198–8.027, $P = 0.020$) were independent risk factors for RFS (Table 4), indicates that patients with combined cN1, grade III, and PR < 20% have poorer RFS.

Disease outcomes

Figure 3 presents the Kaplan-Meier survival curves for the unmatched data, highlighting survival outcomes prior to matching. During the follow-up period, the RFS in the NACT group was noticeably lower than that in the ACT group, with a statistically significant difference ($P < 0.01$). However, after PSM, there was no significant difference in RFS between the two groups ($P = 0.35$) (Fig. 4). The 5-year RFS for the NACT and ACT groups was 74.5% and 67.4%, respectively.

Discussion

In clinical practice, comparing the clinical benefits of different treatment strategies can introduce inherent bias, as treatments are not randomly assigned, potentially leading to skewed results. Studies have shown that survival outcomes in the NACT group are worse than those in the ACT group, consistent with pre-PSM survival analysis[1,12]. This discrepancy is mainly due to differences in clinical and pathological characteristics between the groups. Baseline data indicate that patients with more advanced-stage breast cancer are more likely to receive NACT. PSM reduces these baseline differences, enhancing the reliability of comparisons. This study also examines the prognostic impact of HR+/HER2−low and HR+/HER2−0 subtypes. Univariate analysis reveals that HER2 status is not an independent prognostic factor, aligning with existing literature[13]. Overall, after balancing baseline data with PSM, there was no significant difference in survival outcomes between the NACT and ACT groups, suggesting similar efficacy in HR+/HER2− patients. Even after PSM matching, unmeasured or unaccounted confounding factors may still influence the study results. Therefore, residual confounding could potentially lead to either an underestimation or overestimation of the treatment effect, and caution is warranted when interpreting the findings.

In theory, any patient eligible for adjuvant chemotherapy can receive NACT. Due to the higher aggressiveness of triple-negative breast cancer and HER2 + breast cancer, NACT can improve surgical outcomes and prognosis by controlling the disease early and reducing tumor size[14]. However, NACT's application in HR + breast cancer remains controversial, typically reserved for cases with larger tumor sizes, higher aggressiveness, or lymph node involvement[4,15,16]. This study indicates that lymph node metastasis, low PR expression, and higher grade are independent risk factors for RFS, providing clinicians with additional prognostic indicators for more precise

	HR	95.0% CI for Exp(B)		P
		Lower	Upper	
Chemotherapy(NACT vs. ACT)	0.528	0.210	1.664	0.320
Menopausal status (pre/peri-menopausal vs. post-menopausal)	0.673	0.863	12.080	0.082
Age (years)				0.427
≤ 35 Ref				
36–64	1.307	0.038	6.426	0.592
≥ 65	0.790	0.080	1.766	0.215
Tumor sizs				0.971
cT1 Ref				
cT2	1.421	0.070	18.390	0.929
cT3	1.186	0.126	13.142	0.832
Clinical nodal status				0.135
cN0 Ref				
cN1	0.817	0.039	0.966	**0.045**
cN2-3	0.627	0.139	1.620	0.234
Surgery of the breast (post-menopausal vs. mastectomy)	1.022	0.083	4.537	0.631
Surgery of the axilla(SLNB vs. ALND)	862.450	0.000	0.000	0.989
Histologic subtype	1.030	0.229	13.016	0.595
Grade				**0.003**
I–II Ref				
III	0.936	0.007	0.262	**0.001**
Unknow	0.822	0.028	0.690	**0.016**
ER (< 10% vs. ≥ 10%)	0.953	0.154	6.461	0.998
PR (< 20% vs. ≥ 20%)	0.540	1.744	14.486	**0.003**
CerbB2 (− vs. +/++)	0.731	0.238	4.187	0.999
Ki67 (< 30% vs. ≥ 30%)	0.588	0.322	3.223	0.975

Table 3. Univariate analysis of prognostic factors affecting RFS in PSM cohort. *NACT* neoadjuvant chemotherapy, *ACT* adjuvant chemotherapy, *SLNB* sentinel lymph node biopsy, *ALND* axillary lymph node dissection, *ER* estrogen receptor, *PR* progesterone receptor. Significant values are in (bold).

Variables	HR	95.0% CI for Exp(B)		P
		Lower	Upper	
Menopausal status	0.493	0.885	6.119	0.087
Clinical nodal status				**0.026**
cN0 Ref				
cN1	0.658	0.046	0.612	**0.007**
cN2-3	0.556	0.135	1.195	0.101
Grade				< **0.001**
I–II Ref				
III	0.683	0.016	0.237	< **0.001**
Unknow	0.547	0.071	0.603	**0.004**
PR	0.485	1.198	8.027	**0.020**

Table 4. Multivariate Cox proportional hazards regression analyses for breast cancer of factors affecting the recurrence-free survival after propensity score matching including sensitivity analyses. *PR* progesterone receptor. Significant values are in (bold).

risk assessments and personalized treatment. Our subgroup analysis showed that age and tumor size did not exhibit significant heterogeneity in treatment effects under the current therapeutic strategies, while lymph node involvement was identified as a significant influencing factor. Positive lymph node status indicates a higher risk of recurrence, often necessitating more aggressive adjuvant treatments, such as the combination of chemotherapy and endocrine therapy, to minimize recurrence risk. High-grade tumors are generally more sensitive to chemotherapy, suggesting the need for a more aggressive treatment approach. Patients with low PR expression, even though the tumor may remain ER-positive, often have reduced sensitivity to endocrine therapy, poorer

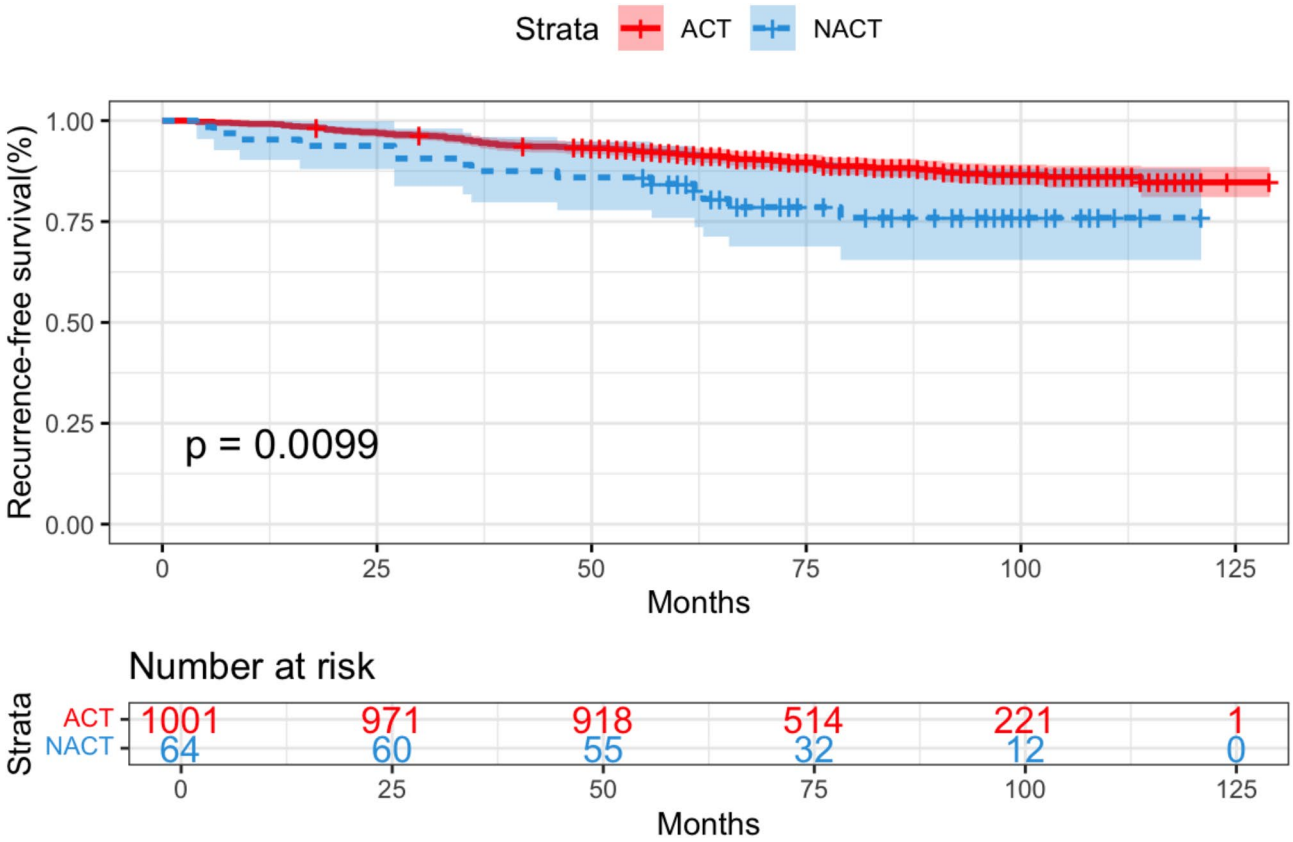

Fig. 3. RFS survival curve of patients in neoadjuvant chemotherapy group and adjuvant chemotherapy group.

prognosis, and a higher likelihood of early recurrence. These patients may respond better to chemotherapy, indicating the need for intensified adjuvant treatment. For all patients, especially those with high-grade tumors, lymph node positivity, or low PR expression, extended endocrine therapy and close monitoring for signs of recurrence are recommended. Patients with lymph node metastasis, low PR expression, and high tumor grade require long-term follow-up and dynamic adjustments to their treatment strategies. While NACT significantly increases the pCR rate and improves prognosis in HER2-positive and TNBC patients, its role in HR+ breast cancer remains unclear. In this study, only 2 out of 47 (4.3%) neoadjuvant chemotherapy patients achieved pCR, making it difficult to explore the impact of pCR on long-term prognosis. In this study, 12/47 (25.5%)patients exhibited stable disease or progression during NACT, indicating poor sensitivity to chemotherapy and a higher risk of recurrence and poor long-term survival. These patients' poor prognosis may reduce the overall RFS of the NACT group. Therefore, in clinical practice, when patients exhibit a poor response to NACT, doctors should promptly adjust treatment plans to prevent delays in surgery. This approach can significantly reduce patient anxiety and improve their overall quality of life. Survival analysis results similar with those of Valachis et al., who also found no significant improvements in distant disease-free survival or overall survival for HR + breast cancer patients treated with NACT[17].

NACT's poor efficacy in HR+/HER2− breast cancer may be linked to the biological characteristics of this subtype. HR + breast cancer tends to proliferate slowly and is less sensitive to chemotherapy[18]. Moreover, NACT works by rapidly killing proliferating cancer cells to shrink tumor size, a mechanism less effective in slow-proliferating HR + cancers. Recent advances in neoadjuvant therapy for HR+/HER2− breast cancer suggest that combining endocrine therapy with targeted therapies such as CDK4/6 inhibitors may offer promising alternatives to neoadjuvant therapy. Clinical trials exploring these combinations are currently underway and may provide better outcomes for HR+/HER2− breast cancer patients[19–21]. Future clinical decisions should be based on individual patient characteristics, and more predictive biomarkers for NACT efficacy should be explored to provide more precise treatment plans for HR + breast cancer patients[22].

As a single-center study with a small sample size, the generalizability of the results is limited, and the statistical power is reduced, increasing the likelihood of selection bias and random error. Although we employed the propensity score matching (PSM) method to maximize balance in baseline characteristics across measured variables and to reduce the impact of confounders on our study results, we acknowledge that this approach cannot completely eliminate the influence of unmeasured variables. These unmeasured variables may include, but are not limited to, patient comorbidities, individual treatment preferences, physician clinical decision-making biases, and other factors that could affect treatment decisions and outcomes.If a treatment group is associated with a higher burden of comorbidities, this could lead to a poorer health status within that group, consequently affecting treatment effects and survival outcomes. Conversely, some physicians might prioritize

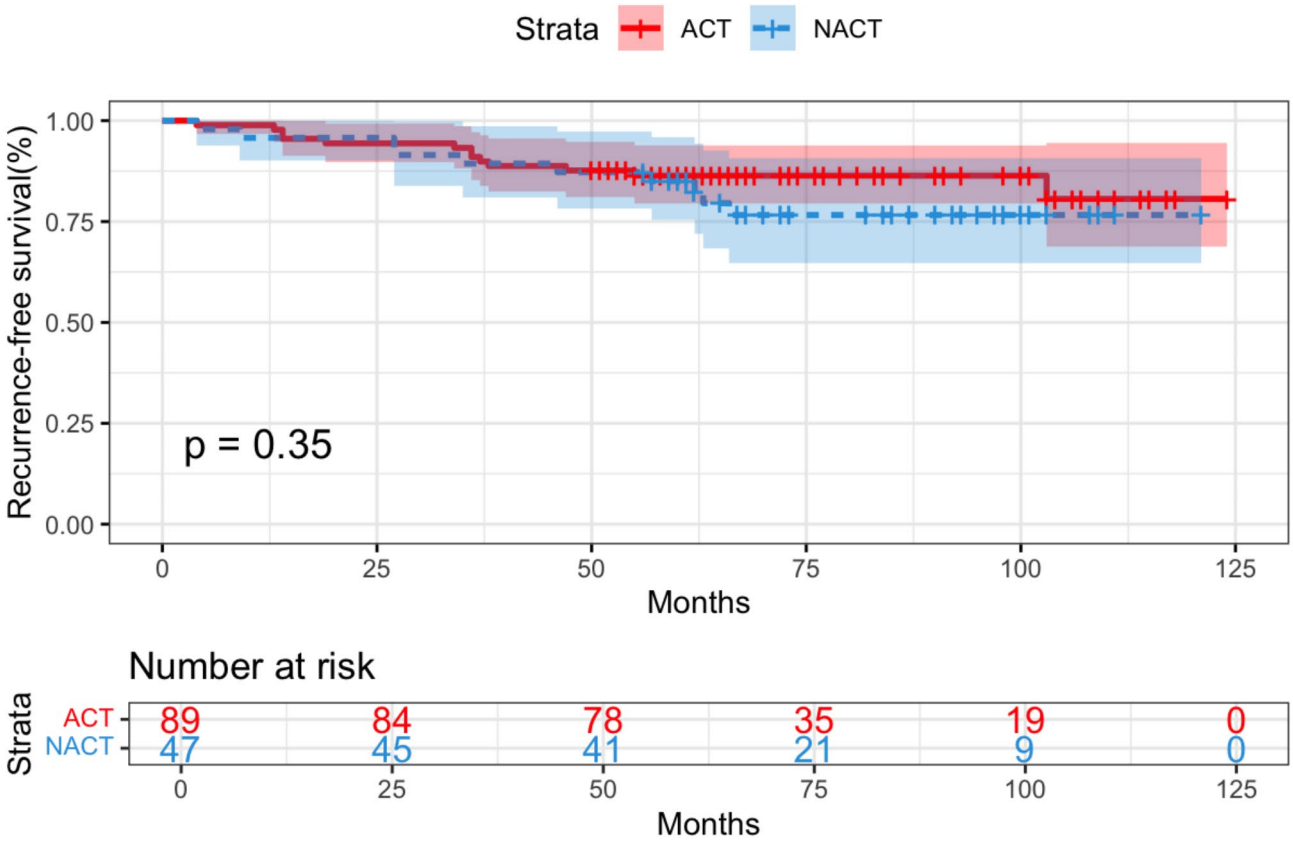

Fig. 4. RFS survival curve of patients in neoadjuvant chemotherapy group and adjuvant chemotherapy group after propensity score.

treatment decisions towards better survival quality, while others may lean towards longer survival. If physician clinical decision biases are not taken into account, this could introduce disparities between different treatment groups, thereby influencing survival outcomes. Due to the unavailability of relevant data sources in this study, we are unable to further analyze the impact of these factors. To mitigate this potential bias, future research could further validate the causal relationship between treatment effects and survival outcomes through more refined patient selection, incorporating more variables, and considering randomized controlled trials. Although the median follow-up was 67 months, HR+/HER2− breast cancer is known for late recurrences, typically occurring 5–10 years post-surgery[2]. Short-term follow-up may not fully capture the disease's long-term prognosis, requiring continued follow-up to assess recurrence events. Specifically, the insufficient follow-up time may lead to an underestimation of recurrence risk, particularly in subgroups of patients where late recurrence is more common, such as HR+/HER2− patients. This limitation may partially affect the comprehensiveness of our conclusions. Therefore, our results should be interpreted primarily as an assessment of recurrence risk within the median follow-up period, rather than a complete evaluation of long-term recurrence risk. While PSM was used to reduce confounding factors, prospective studies are needed to further validate NACT's utility in HR+/HER2− breast cancer. Additionally, excluding patients who did not complete NACT could introduce bias, as these patients were likely less responsive to chemotherapy. This study also lacked genetic testing, a crucial component in precision breast cancer treatment, particularly in assessing sensitivity to NACT and predicting prognosis. Genetic testing, such as the 21-gene or 70-gene assays, can predict chemotherapy response, helping clinicians decide whether NACT should be the primary treatment[23,24]. In the absence of genetic testing, identifying which HR+/HER2− patients would benefit from chemotherapy becomes difficult, potentially leading to overtreatment or undertreatment. The absence of genetic testing data in our study may introduce certain limitations to the practical application of our findings, particularly in the development of personalized treatment strategies. Genetic testing can also help differentiate breast cancer subtypes and biological characteristics. For hormone receptor-positive breast cancer patients, it helps determine those suitable for NACT and those better suited for surgery or endocrine therapy. Without such testing, treatment plans may lack precision, impacting long-term prognosis. Genetic testing also predicts recurrence risk, aiding in developing long-term treatment strategies. Without it, high-risk patients may miss opportunities for adequate preoperative treatment.

Since this study's enrollment period was early, it did not assess the impact of combining NACT with neoadjuvant endocrine therapy, possibly reducing the relevance of its findings for personalized treatment. Future studies should consider incorporating neoadjuvant endocrine therapy to better assess optimal strategies for HR+/HER2− breast cancer patients.

Although current research has not demonstrated a prognostic advantage of NACT in HR+/HER2− breast cancer, further studies are necessary. Specifically, studies with longer follow-up periods and larger sample sizes may better validate NACT's potential effects in specific patient subgroups. Future research should also focus on therapeutic targets in treatment decision-making to develop more individualized treatment strategies. Due to the similarity in survival benefits between neoadjuvant chemotherapy and adjuvant chemotherapy, clinicians can choose the most appropriate treatment timing based on the patient's specific condition. For patients with larger or locally advanced tumors, neoadjuvant chemotherapy may be more suitable for shrinking the tumor and improving surgical resectability. On the other hand, adjuvant chemotherapy may be more appropriate for patients with smaller tumors or early-stage breast cancer.

Conclusions

This study found no significant difference in RFS between neoadjuvant and adjuvant chemotherapy for HR+/HER2− breast cancer patients after propensity score matching. Independent risk factors for RFS include clinical nodal status, grade, and PR expression. Given the limited long-term benefits of neoadjuvant chemotherapy, personalized treatment decisions should focus on surgical needs and tumor downstaging. Future research should incorporate genetic testing and biomarkers to enhance treatment precision and guide patient selection for optimal therapeutic outcomes.

Data availability

Te datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Author contributions

ZZ designed the study. ZC and ZY extracted and analyzed the data. ZC and ZD interpreted the evidence and wrote the manuscript. LR and ZZ revised the article. All authors contributed to the article and approved the submitted version.

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Declarations

Competing interests

The authors declare no competing interests.

Additional information

Correspondence and requests for materials should be addressed to Z.Z.

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