Factors influencing pathological complete response to neoadjuvant chemotherapy in resectable breast cancer: A retrospective study

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Abstract. Neoadjuvant chemotherapy (NAC) is widely used to treat breast cancer and a pathological complete response (pCR) following NAC is associated with an optimal prognosis; however, pCR rates vary significantly. In the present study, the effects of clinicopathological factors and the administration of different taxanes on pCR rates in patients with resectable breast cancer were assessed. A total of 552 patients with breast cancer who received NAC between May 2019 and June 2024 were included in the present study. The clinicopathological traits of the patients were retrieved from medical records and their association with the pCR rate was evaluated using univariate and multivariate regression analyses. The efficacy of nanoparticle albumin-bound (Nab)-paclitaxel, docetaxel and paclitaxel liposomes in different subtypes of breast cancer were further evaluated. A total of 189 of 552 (34.2%) patients achieved pCR following NAC. The pCR rate varied significantly among different molecular subtypes as follows: 58.9% (96/163), 40.7% (37/91), 35.6% (37/104) and 9.8% (19/298) among patients with hormone receptor (HR) negative (-) human epidermal growth factor receptor 2 (HER2) positive (+), HR^+HER2^+, HR^-HER2^- and HR^+HER2^- breast cancer, respectively. The factors estrogen receptor (ER), progesterone receptor and HER2 status, Ki-67 index and taxane regimen were all significantly associated with pCR in the univariate analysis. In the multivariate regression analysis, ER^-, $HER2^+$, Ki-67 index ≥30% and Nab-paclitaxel were independent predictors of pCR. The multivariate regression analysis model had an area under the receiver operating characteristic curve area under the curve of 0.774 (95% confidence interval, 0.735-0.813). The pCR rates were 41.3, 38.2 and 25.1% among the Nab-paclitaxel, docetaxel and paclitaxel liposome groups, respectively. Patients with ER^-, $HER2^+$, Ki-67 index ≥30% were associated with high pCR rates. Moreover, patients who received Nab-paclitaxel and docetaxel were more likely to achieve pCR compared with paclitaxel liposomes, particularly for those with $HER2^+$ and HR^-HER2^- statuses. In conclusion, molecular subtypes (ER/HER2 status, high Ki-67) and different taxanes significantly influence pCR likelihood. Nab-paclitaxel and docetaxel were identified as effective taxanes, highlighting their potential clinical preference, especially in $HER2^+$ and HR^-HER2^- breast cancer.

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Introduction

Breast cancer is one of the most common cancer types worldwide, including in China; it has an incidence rate of ~60 cases in 10,000, which ranks second among all cancer types and mortality rate of 11 in 10,000 cases, which ranks fifth among female tumors (1,2). The incidence of breast cancer continues to rise; it is estimated that numerous people will be diagnosed with breast cancer in the next decades (3). Neoadjuvant chemotherapy (NAC), initially introduced in the 1970s, has become a widely employed therapeutic approach for patients with operable and locally advanced breast cancer (4). NAC has demonstrated efficacy in improving the rate of breast-conserving surgery and obviating the need for axillary lymph node dissection via tumor downstaging, particularly among patients with human epidermal growth factor receptor 2 (HER2) positive (+) status (5-7). Furthermore, NAC can provide valuable information on the drug sensitivity of diverse chemotherapy regimens, thereby facilitating the guidance of subsequent treatment strategies (8).

Pathological complete response (pCR) rate is the standard for evaluating the efficacy of NAC. The pCR rate among different subtypes of breast cancer ranges from 2 to 68% (9). The prognosis of patients achieving pCR is significantly

improved compared with that of patients with residual cancer burden, leading to prolonged survival and reduced risk of distant metastasis (10). For patients with invasive breast cancer, such as triple-negative and $HER2^+$ types, attaining a pCR is closely associated with long-term clinical benefit (11). The prediction of the patients who will achieve pCR could guide personalized treatment based on clinical and pathological factors. Numerous studies have explored the relationship between patient characteristics, clinical tumor stage, lymph node status, HER2 status and hormonal receptor status with pCR in patients with breast cancer who have been treated with NAC (12-14). A previous retrospective study indicated that age and subtypes of breast cancer were associated with pCR; following NAC, patients with younger age, luminal B2 $HER2^+$, HER2 upregulation and triple-negative subtype were more likely to achieve pCR (15). By contrast, another study indicated that only clinical tumor stage, progesterone receptor (PR) negative (-) status and $HER2^+$ status were associated with pCR, while age, clinical lymph node stage, estrogen receptor (ER) status and Ki-67 index indicated no significant correlation (16). Furthermore, the findings of a real-world study involving 7,711 patients differed from those reported in the aforementioned study, as clinical lymph node stage, ER, PR, HER2 status, Ki-67 index and NAC treatment cycle correlated with pCR (17). The findings from various studies regarding the factors influencing pCR exhibit considerable variability. Therefore, additional research is required to clarify the factors influencing pCR.

Anthracycline plus taxane regimens serves as the cornerstone regimen for both neoadjuvant and adjuvant treatment of breast cancer, effectively reducing recurrence and mortality (18). Taxanes are antitumor drugs isolated from plants; it includes mainly paclitaxel, docetaxel, nanoparticle albumin-bound (Nab)-paclitaxel and paclitaxel liposome, which are essential agents used in NAC regimens (19). The National Comprehensive Cancer Network guidelines (version 3; 2024) (20) recommend paclitaxel and docetaxel as preferred taxane agents and Nab-paclitaxel which may be substituted with paclitaxel or docetaxel due to medical necessity (such as a hypersensitivity reaction). Paclitaxel is the standard drug for NAC used for breast cancer; however, paclitaxel injection can cause severe allergic reactions in 10-40% of patients (21). Due to these side effects, Nab-paclitaxel, liposomal paclitaxel and docetaxel have emerged as alternatives (18,22). Although the toxicity profiles of Nab-paclitaxel and paclitaxel liposomes are reduced, the differences in the efficacy of Nab-paclitaxel, paclitaxel liposomes and paclitaxel and docetaxel in breast cancer are currently uncertain. Therefore, additional studies are required to confirm their efficacy in NAC.

The present study aimed to evaluate clinicopathological data collected from patients with breast cancer following NAC to analyze the associations of age, tumor location, clinical stage, lymph node involvement, ER, PR, HER2 status, Ki-67 index and taxane regimen with pCR rate. Furthermore, the efficacy of Nab-paclitaxel, docetaxel and paclitaxel liposomes was evaluated in different subtypes of breast cancer following NAC.

Materials and methods

Patient selection. In July 2024, medical records of patients with breast cancer who were treated with NAC and adjuvant radiotherapy in Nanchang People's Hospital (Nanchang, China) and Affiliated Rehabilitation Hospital of Nanchang University (Nanchang, China) during May 2019 and June 2024 were reviewed. The present study included a total of 552 patients with invasive breast cancer who were diagnosed by core needle biopsy and received NAC and radiotherapy during this period. The clinical stage of all patients prior to NAC was evaluated using breast ultrasonography, chest computerized tomography and breast magnetic resonance imaging. All patients underwent lumpectomy or mastectomy and axillary lymph node dissection following completion of the planned NAC dosage. Patients with bilateral breast cancer or prior history of cancer were excluded from the present study. The present study was approved by the Institutional Review Board ethics committee of Nanchang People's Hospital (approval no. K-kt2024005; Nanchang, China) from which the patients were enrolled. The requirement for patient approval or written informed consent was waived due to the retrospective nature of the present study.

NAC regimens. The NAC regimens were selected according to the subtypes of breast cancer. Breast cancer samples with ≥10% of ER or PR positive tumor nuclei were defined as ER^+ or PR^+, since primary breast cancer with ER 1-9% positivity shows similar clinical behavior to ER 1% (23). HER2 protein upregulation was assessed using immunohistochemical analysis; 3 or 2+ with HER2 gene amplification assessed using *in situ* hybridization was defined as $HER2^+$. The treatment options for patients with HR^+HER2^- and HR^-HER2^- included four cycles of anthracyclines and cyclophosphamide followed by four cycles of taxanes (AC-T), six cycles of taxanes, anthracyclines and cyclophosphamide (TAC) and six cycles of taxanes and carboplatin (Tcb). The regimens for patients with $HER2^+$ breast cancer were composed of four cycles of anthracyclines and cyclophosphamide followed by four cycles of taxanes with trastuzumab or trastuzumab and pertuzumab (AC-TH/AC-THP), six cycles of taxanes and carboplatin with trastuzumab or trastuzumab and pertuzumab (TcbH/TcbHP) and six cycles of taxanes with trastuzumab and pertuzumab (THP). Regarding taxane-based regimens, liposomal paclitaxel was administered in both weekly and tri-weekly regimens.

Assessment of pathological response. pCR was defined as the absence of invasive disease in both primary tumor and lymph nodes and the presence of *in situ* cancer following treatment in the absence of residual invasive disease (ypT0/is ypN0), as per the 8th Edition of American Joint Committee on Cancer Staging Manual (24).

Statistical analysis. The data were analyzed using the SPSS software (version 23; IBM Corp.). Categorical variables age, tumor location, clinical tumor stage, Ki-67 index, molecular subtypes of breast cancer, chemotherapy regimens, taxanes and lymph node, ER, PR and HER2 status were described by percentage. The differences in pCR rate for these variables was analyzed using the χ^2 or Fisher's exact tests. With the exception of the subtypes of breast cancer and the chemotherapeutic regimens, the other variables were considered as alternative variables with $P<0.05$ in the univariate analysis. In multivariate analysis, binary regression analysis was used to analyze the role of these variables in predicting pCR. A prediction model

was established using the results of the multivariate logistic regression analysis, and receiver operating characteristic (ROC) curve analysis was used to assess the prediction power of the model. P<0.05 was considered to indicate a statistically significant difference. All charts were generated using the GraphPad Prism software (version 9.5; Dotmatics).

Results

Study population and treatment regimen distribution. The clinicopathological and treatment characteristics of the enrolled 552 patients were analyzed (Table I). Overall, 274 (49.6%) patients were ER- and 366 (66.3%) patients were PR-. A total of 433 (78.4%) patients exhibited a Ki-67 index >30% and 254 (46.0%) patients were $HER2^+$. The distribution of the molecular subtypes among the enrolled patients is shown in Fig. 1A. A total of 200 (36.2%) patients received the AC-T regimen, 82 (14.9%) patients received the TAC regimen, 16 patients (2.9%) received the Tcb regimen, 48 (8.7%) patients received the THP regimen, 23 (4.2%) patients received the AC-TH/TcbH regimen, 31 (5.6%) patients received the AC-THP regimen and 152 (27.5%) patients received the TcbHP regimen. Among the taxane-based regimens, 167 (30.3%) patients received Nab-paclitaxel, 178 (32.2%) patients received docetaxel and 207 (37.5%) patients received paclitaxel liposomes.

Overall and subtype-specific pCR rates. Overall, 189 of 552 (34.2%) patients achieved pCR. The pCR rates of different subtypes varied as follows: 58.9% (96/163), 40.7% (37/91), 35.6% (37/104) and 9.8% (19/298) for the patient groups of HR^-HER2^+, HR^+HER2^+, HR^-HER2^- and HR^+HER2^-, respectively (Fig. 1B; P<0.001). Following univariate analysis, the results indicated that pCR was more likely to be achieved in patients with ER^- [49.3 vs. 19.7%; odds ratio (OR)=4.029; 95% confidence interval (CI), 2.755-5.891; P<0.001] and PR^- breast cancer (43.2 vs. 16.7%; OR=3.798; 95% CI, 2.452-5.883; P<0.001). Compared with patients with $HER2^-$ breast cancer, the $HER2^+$ group exhibited a significantly increased pCR rate (52.4 vs. 18.8%; OR=4.750; 95% CI, 3.245-6.952; P<0.001). In addition, the Ki-67 ≥30% group also exhibited a significantly increased pCR rate compared with the Ki-67 <30% group (40.9 vs. 10.1%; OR=6.165; 95% CI, 3.294-11.537; P<0.001; Fig. 2). The pCR rates were compared among different types of taxanes. The pCR rates of Nab-paclitaxel, docetaxel and paclitaxel liposomes were 41.3, 38.2 and 25.1%, respectively (P=0.002; Fig. 3). The pCR rates of Nab-paclitaxel (OR=2.099; 95% CI, 1.352-3.258; P=0.001) and docetaxel (OR=1.843; 95% CI, 1.192-2.850; P=0.001) were significantly increased compared with those who received paclitaxel liposomes. No significant differences were observed in the pCR rates when patients were stratified by age, tumor location, clinical T stage and lymph node status (Table II).

Comparative efficacy of taxane-based regimens. The pCR rates of different taxanes were analyzed among different molecular subtypes of breast cancer. The results demonstrated no significant difference in the pCR rate among the paclitaxel liposomes, Nab-paclitaxel and docetaxel (9.4 vs. 8.2 vs. 12.2%; P=0.78) in HR^+HER2 group $^-$. For patients that were $HER2^+$, Nab-paclitaxel (64.4%) had the highest pCR rate compared with patients who received docetaxel (47.3%; P=0.024) or paclitaxel liposomes (47.89%; P=0.047). In the HR^-HER2^- group, no significant difference was observed in the pCR rates between docetaxel and Nab-paclitaxel treatments (52.63 vs. 40.00%; P=0.354); however, the pCR rate of the docetaxel group was significantly increased compared with that the paclitaxel liposomes group (52.63 vs. 22.50%; P=0.024; Table III and Fig. 3). Overall, both Nab-paclitaxel and docetaxel subgroups demonstrated increased pCR rates among patients that were HR^-HER2^-, while Nab-paclitaxel demonstrated the highest pCR rate in patients that were $HER2^+$. By contrast, the paclitaxel liposome group had the lowest pCR rate overall, and there was no efficacy advantage in any subtypes of breast cancer.

Development and validation of a pCR predictive model. Based on the results of univariate analysis, variables with statistical significance were included, such as ER status, PR status, HER2 status, Ki-67 index and taxane regimen were used to establish a model to predict pCR. A multivariate regression analysis was performed on the variables with P<0.05 from the univariate analysis. The results indicated that the patients that achieved pCR were associated with the following characteristics: ER^-, Ki-67 ≥30% and $HER2^+$ with regard to tumor features, and taxane regimen with Nab-paclitaxel with regard to treatment administration (Table II). Based on the clinically and statistically significant variables, a model was constructed to predict pCR for patients with breast cancer treated with NAC. The area under the curve value of the ROC curve of the model was 0.774 (95% CI, 0.735-0.813; Fig. 4), which indicated that the model exhibited acceptable discriminatory power in predicting pCR. The cut-off value of this model was 0.5, with a sensitivity of 50.26% and a specificity of 82.92% (Table IV). The positive predictive value was 60.51%, negative predictive value was 76.20% and correction rate was 71.74%.

Discussion

NAC has become a widely employed therapeutic approach for patients with operable and locally advanced breast cancer (25). pCR has been applied to evaluate the efficacy of NAC. Breast cancer is a heterogeneous malignancy with distinct subtypes exhibiting varied responses to NAC. The pCR rate among different breast cancer subtypes varies significantly. The patients who achieve pCR exhibit an optimal prognosis compared with those with residual cancer burden (26). However, the prediction of pCR is challenging.

To assess the predictive value of the clinicopathological factors and different types of taxanes in predicting pCR following NAC in breast cancer, the present study conducted a retrospective analysis on patients with breast cancer who received NAC. A predictive model was developed based on the clinicopathological characteristics to estimate the rates of pCR. In the present study, distinct sensitivities were observed with regard to NAC among various subtypes of breast cancer. The highest rate of pCR was achieved in the $HER2^+$ group, followed by those in the HR^-HER2^- group and patients with HR^+HER2^- who exhibited the lowest pCR rate, which was just 9.8% indicating that HR^+HER2^- subtype breast cancer was not sensitive to chemotherapy. It was reported that patients with the HR^+HER2^- subtype of breast cancer

Table I. Baseline characteristics of 552 patients who achieved pCR (n=189) and non-pCR (n=363).

Variable	Non-pCR, n (%)	pCR, n (%)	Total, n	P-value
Age, years				0.477
≤35	48 (69.6)	21 (30.4)	69	
>35	315 (65.2)	168 (34.8)	483	
Tumor location				0.795
Left	179 (66.3)	91 (33.7)	270	
Right	184 (65.2)	98 (34.8)	282	
Tumor location, quadrant				0.872
Upper outer	198 (65.1)	106 (34.9)	304	
Lower outer	42 (63.6)	24 (36.4)	66	
Upper inner	69 (69.7)	30 (30.3)	99	
Lower inner	17 (60.7)	11 (39.3)	28	
Center	37 (67.3)	18 (32.7)	55	
cT stage				0.755
cT1	13 (65.0)	7 (35.0)	20	
cT2	222 (65.3)	118 (34.7)	340	
cT3	82 (69.5)	36 (30.5)	118	
cT4	46 (62.2)	28 (37.8)	74	
Lymph node status				0.104
Negative	26 (78.8)	7 (21.2)	33	
Positive	337 (64.9)	182 (35.1)	519	
ER status				<0.001
Negative	139 (50.7)	135 (49.3)	274	
Positive	224 (80.6)	54 (19.4)	278	
PR status				<0.001
Negative	208 (56.8)	158 (43.2)	366	
Positive	155 (83.3)	31 (16.7)	186	
Ki-67 index				<0.001
<30%	107 (89.9)	12 (10.1)	119	
≥30%	256 (59.1)	177 (40.9)	433	
HER2 status				<0.001
Negative	242 (81.2)	56 (18.8)	298	
Positive	121 (47.6)	133 (52.4)	254	
Molecular subtype				<0.001
HR^+HER2^-	175 (90.2)	19 (9.8)	194	
HR^-HER2^+	67 (41.1)	96 (58.9)	163	
HR^+HER2^+	54 (59.3)	37 (40.7)	91	
HR^-HER2^-	67 (64.4)	37 (35.6)	104	
NAC regimen				<0.001
AC-T	164 (82.0)	36 (18.0)	200	
TAC	66 (80.5)	16 (19.5)	82	
Tcb	12 (75.0)	4 (25.0)	16	
THP	24 (50.0)	24 (50.0)	48	
AC-TH + TcbH	16 (69.6)	7 (30.4)	23	
AC-THP	15 (48.4)	16 (51.6)	31	
TcbHP	66 (43.4)	86 (56.6)	152	
Taxanes				0.002
Paclitaxel liposome	155 (74.9)	52 (25.1)	207	
Nab-paclitaxel	98 (58.7)	69 (41.3)	167	
Docetaxel	110 (61.8)	68 (38.2)	178	

AC-T, anthracyclines and cyclophosphamide followed by taxanes; TAC, taxanes, anthracyclines and cyclophosphamide; Tcb, taxanes and carboplatin; THP, taxanes with trastuzumab and pertuzumab; TcbH, taxanes and carboplatin with trastuzumab; TcbHP, TcbH with pertuzumab; AC-TH; taxanes with trastuzumab; AC-THP, AC-TH and pertuzumab; cT, clinical tumor; Nab, nanoparticle albumin-bound; ER, estrogen receptor; PR, progesterone receptor; pCR, pathological complete response; HR, hormone receptor; HER, human epidermal growth factor receptor.

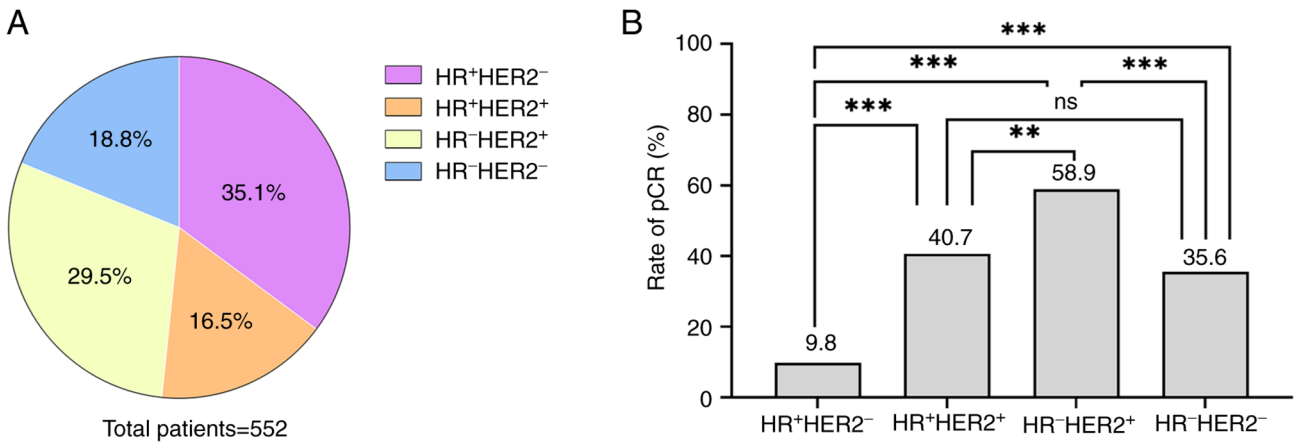

Figure 1. Distribution of molecular subtypes and pCR rates in patients with breast cancer. (A) The distribution of different molecular subtypes of breast cancer among the patients enrolled; (B) The overall pCR rates among different molecular subtypes of breast cancer in pairwise comparisons. **P<0.01; ***P<0.001. ns, not significant; pCR, pathological complete response; HR, hormone receptor; HER, human epidermal growth factor receptor.

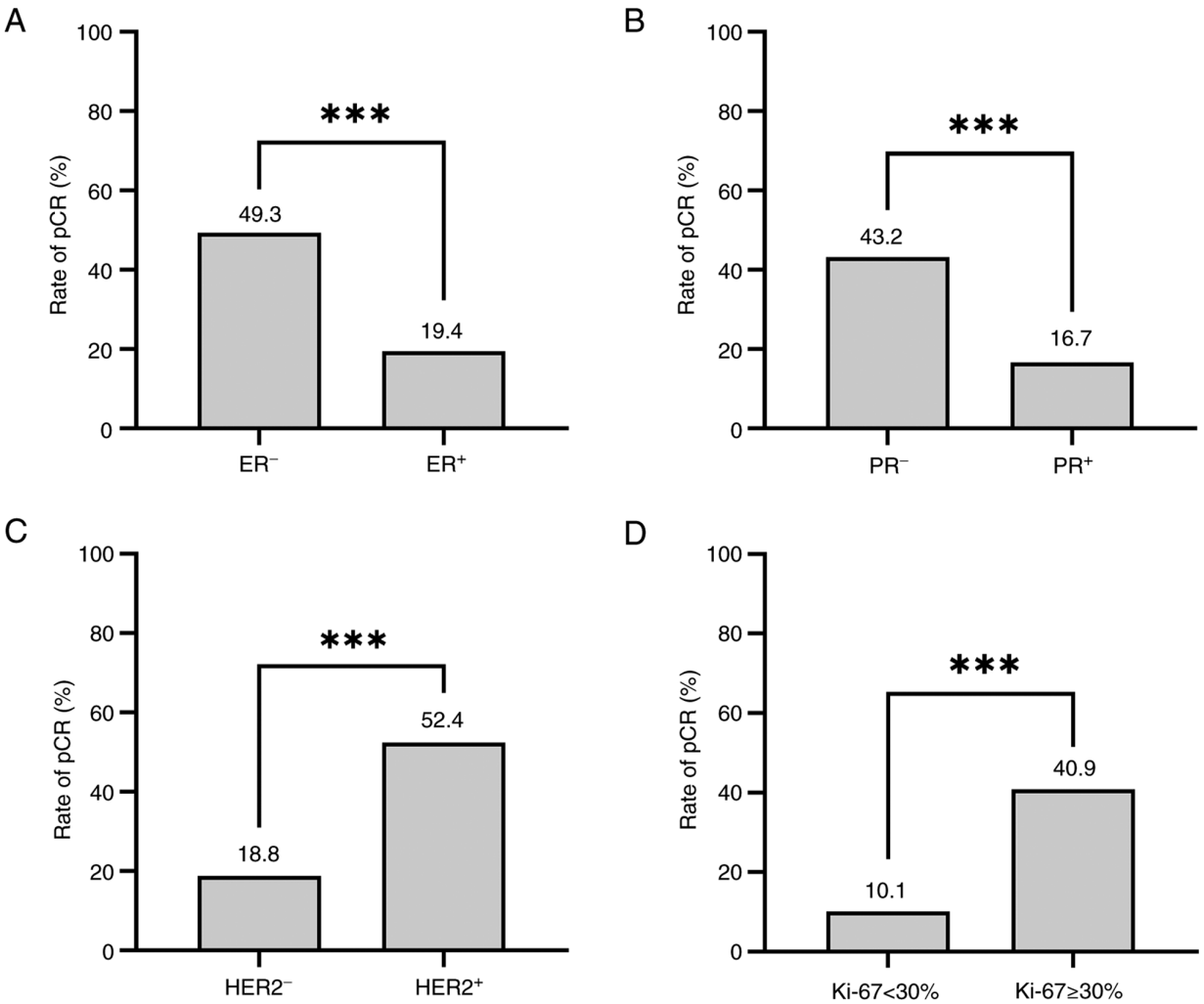

Figure 2. pCR rates stratified by ER, PR, HER2, and Ki-67 status. (A) pCR rates in patients with different ER status; (B) pCR rates in patients with different PR status; (C) pCR rates in patients with different HER2 status; (D) pCR rates in patients with different Ki-67 status. ***P<0.001. pCR, pathological complete response; HR, hormone receptor; HER, human epidermal growth factor receptor; ER, estrogen receptor; PR, progesterone receptor.

demonstrated a low response rate to NAC regimens containing taxanes and anthracyclines with pCR rates ranging from 0 to 15%, consistent with the findings of the present study (27-29). In addition, the present univariate regression analysis found that ER, PR and HER2 status, Ki-67 index, and taxane regimen were significantly associated with pCR.

Table II. Univariate and multivariate analysis for pathologic complete response.

	Univariate analysis			Multivariate analysis		
Variable	OR	95% CI	P-value	OR	95% CI	P-value
Age, years			0.477			
≤35	Reference	-				
>35	1.219	0.705-2.104				
Tumor location			0.795			
Left	Reference	-				
Right	1.048	0.737-1.489				
Tumor location, quadrant			0.872			
Upper outer	Reference	-				
Lower outer	1.067	0.613-1.858				
Upper inner	0.812	0.498-1.325				
Lower inner	1.209	0.546-2.674				
Center	0.909	0.493-1.674				
cT stage			0.755			
cT1	Reference	-				
cT2	0.987	0.383-2.541				
cT3	0.815	0.300-2.214				
cT4	1.130	0.403-3.173				
Lymph node status			0.104			
Negative	Reference					
Positive	2.006	0.854-4.711				
ER status			<0.001			
Negative	4.029	2.755-5.891		2.161	1.238-3.77	0.007
Positive	Reference	-		Reference	-	
PR status			<0.001			
Negative	3.798	2.452-5.883		1.386	0.727-2.643	0.322
Positive	Reference	-		Reference	-	
Ki-67 index			<0.001			
<30%	Reference	-		Reference	-	
≥30%	6.165	3.294-11.537		3.741	1.917-7.301	<0.001
HER2 status			<0.001			
Negative	Reference	-		Reference	-	
Positive	4.750	3.245-6.952		3.662	2.419-5.545	<0.001
Taxane			0.002			
Paclitaxel liposome	Reference	-		Reference	-	
Nab-paclitaxel	2.099	1.352-3.258	0.001	1.647	1.007-2.695	0.047
Docetaxel	1.843	1.192-2.850	0.006	1.093	0.666-1.795	0.725

OR, odds ratio; Nab, nanoparticle albumin-bound; cT, clinical tumor; ER, estrogen receptor; PR, progesterone receptor; HER, human epidermal growth factor receptor.

Targeted therapy combined with chemotherapy is the standard treatment for patients with $HER2^+$ breast cancer (20). Clinical trials, such as NeoSphere, NeoALTTO and KRISTINE have demonstrated that the integration of trastuzumab and pertuzumab with chemotherapy yields a high response rate, achieving a pCR rate of up to 55% (6,10,30). The present study found that patients with $HER2^+$ breast cancer were associated with a high pCR rate, especially patients with HR^-HER2^+ breast cancer, which reached 58.9%.

HR^-HER2^- breast cancer was also more sensitive to chemotherapy compared with the HR^+HER2^- subtypes, as reported by the CALGB 40603 study, with a pCR rate of 44% for patients who received the TAC regimen; the I-SPY2 study reported a pCR rate of 26% in patients who received the T-AC regimen and the BrighTNess study reported a pCR rate of

Table III. Pathological complete response rates of types of taxane among molecular subtypes of breast cancer.

Variable	Non-pCR, n (%)	pCR, n (%)	Total, n	Odds ratio	95% CI	P-value
HR^+HER2^-						
Paclitaxel liposome	87 (90.6)	9 (9.4)	96	Reference		0.781
Nab-paclitaxel	45 (91.8)	4 (8.2)	49	0.85	0.25-2.94	0.809
Docetaxel	43 (87.8)	6 (12.2)	49	1.34	0.45-4.03	0.592
$HER2^+$						
Nab-paclitaxel	26 (35.6)	47 (64.4)	73	Reference		0.054
Docetaxel	58 (52.7)	52 (47.3)	110	0.496	0.270-0.911	0.024
Paclitaxel liposome	37 (52.1)	34 (47.9)	71	0.508	0.261-0.991	0.047
HR^-HER2^-						
Docetaxel	9 (47.4)	10 (52.6)	19	Reference		0.062
Nab-paclitaxel	27 (60.0)	18 (40.0)	45	0.6	0.203-1.767	0.353
Paclitaxel liposome	31 (77.5)	9 (22.5)	40	0.261	0.081-0.839	0.024

Nab, nanoparticle albumin-bound; HR, hormone receptor; HER, human epidermal growth factor receptor.

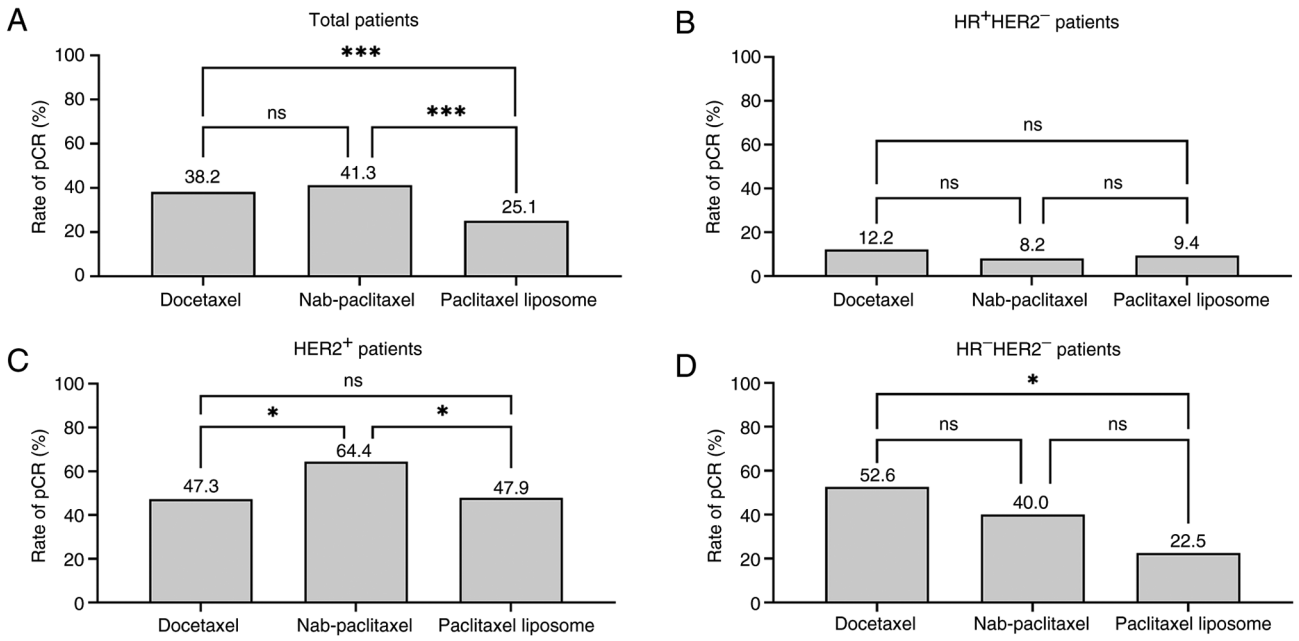

Figure 3. pCR rates of different taxanes among different molecular subtypes of breast cancer. The pCR rates of (A) total patients, and patients with (B) HR^+HER2^-, (C) $HER2^+$ and (D) HR^-HER2 patients. $^*P<0.05$; $^{***}P<0.001$. ns, not significant; pCR, pathological complete response; HR, hormone receptor; HER, human epidermal growth factor receptor; Nab, nanoparticle albumin-bound.

58% in patients who received the Tcb regimen (15,31,32). In the present study, AC-T, TAC and Tcb were used as NAC regimens, with an overall pCR rate of 35.6%, which was similar to that reported by aforementioned studies. Immunotherapy may also improve pCR rate in TNBCs (33). However, only 1 in 104 patients that were HR^-HER2^- used pembrolizumab in combination with Nab-paclitaxel and carboplatin in the present cohort (treated May 2019 and June 2024) as local health insurance policies did not cover the treatment until late 2023 in the present center and the patient achieved pCR. As it was only an individual case in the present cohort, the case was not analyzed separately, which reflects a limitation of the present study.

Dou *et al* conducted a study of 879 breast cancer cases treated with NAC, reporting a significantly increased rate of pCR in patients who were ER^-/PR^- compared with that of patients with ER^+/PR^+ (64.6 vs. 21.5%; P<0.001) (34). The findings of the present study also indicated that patients with ER^- or PR^- breast cancer exhibited a higher likelihood of achieving pCR. Although univariate analysis indicated a notable association between PR and pCR, the multivariate analysis did not demonstrate any significant associations.

A previous study reports that 15-20% of breast cancer cases exhibit amplification of HER2, resulting in an upregulation of HER2 (35). The homo- or hetero-dimerization of HER2 with one of the other three receptors (HER1 or EGFR, HER3 and

Table IV. Sensitivity and specificity of the model for pCR.

Classification	Predicted non-pCR, n	Predicted pCR, n	Total, n
Observed non-pCR	301	62	363
Observed pCR	94	95	189
Total	395	157	552

Cut-off value, 0.5; sensitivity, 50.26%; specificity, 82.92%; positive predictive value, 60.51%; negative predictive value, 76.20%; correction rate, 71.74%. pCR, pathological complete response.

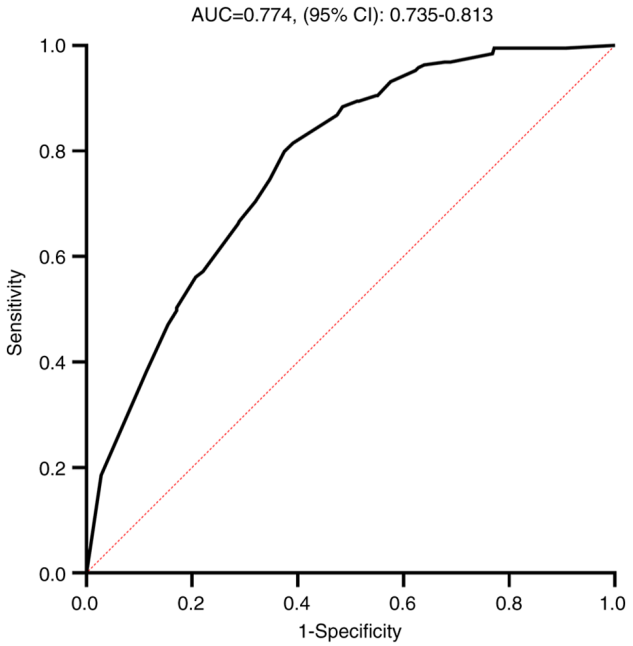

Figure 4. ROC curve of the prediction model pCR. The variables ER$^+$, PR$^+$, HER2$^-$, Ki-67 ≤30% and liposomal paclitaxel were used as references to produce the ROC curve. ROC, receiver operating characteristic; AUC, area under curve; pCR, pathological complete response; HR, hormone receptor; HER, human epidermal growth factor receptor; ER, estrogen receptor; PR, progesterone receptor.

HER4) triggers the activation of signaling pathways which promote cancer cell proliferation, invasion and survival (36). HER2 status is positively correlated with the pCR rate in breast cancer cases treated with NAC (37). The present study demonstrated a significantly higher pCR rate in patients with HER2$^+$ breast cancer.

The Ki-67 index also exhibits important predictive value in breast cancer cases treated with NAC. Denkert *et al* reported pCR rates of 4.2, 12.8 and 29.0% in patients with a Ki-67 index of ≤15, 15.1-35 and >35%, respectively (38). Another predictive model that examined the response to NAC in breast cancer also demonstrated an association between Ki-67 status and the pCR rate (39). Consistent with these findings, the results of the present study demonstrated that patients with Ki-67 ≥30% expression demonstrated an increased pCR rate compared with those with Ki-67 <30% expression, which highlighted the key predictive value of Ki-67 index in NAC treatment for breast cancer.

Taxanes containing regimens are widely used as NAC for breast cancer. The toxicity profiles of different paclitaxel have been reported in previous publications (40-42). Generally, paclitaxel liposome and Nab-paclitaxel showed relatively mild side effects, especially hypersensitivity reaction. The response rate of breast cancer to NAC may be influenced by different types of taxanes (43). Zhang *et al* (44) conducted a retrospective study on 235 patients with breast cancer treated with NAC and indicated that Nab-paclitaxel demonstrated an advantage in improving the total and axillary-only pCR rate over liposomal paclitaxel. An additional study retrospectively analyzed the efficacy of solvent-based paclitaxel, liposomal paclitaxel, Nab-paclitaxel and docetaxel, which also indicated that the Nab-paclitaxel group exhibited the highest total pCR cases and breast pCR rates (43). The present study demonstrated that the Nab-paclitaxel group achieved the highest pCR rate across all patient cohorts analyzed. Subgroup analyses demonstrated that the Nab-paclitaxel group also exhibited the highest pCR rate in patients with HER2$^+$ breast cancer. By contrast, the docetaxel group demonstrated the highest pCR rate among patients HR$^-$HER2$^-$ breast cancer. However, this difference was not statistically significant compared with that of the Nab-paclitaxel group. Notably, in the HR$^+$HER2$^-$ group, no significant differences in pCR rates were observed among the three treatment groups, which may be due to their inherent insensitivity to chemotherapy. Although paclitaxel liposome exhibits low toxicity profiles, it does not show an advantage in improving pCR in any subtypes of breast cancer (44). Therefore, the selection of taxanes according to breast cancer subtype may improve the pCR rate after NAC.

Based on these findings, a multivariate regression model was used to predict pCR. The model revealed that patients characterized by ER$^-$, Ki-67 index ≥30%, HER2$^+$ and taxane regimen with Nab-paclitaxel were more likely to achieve pCR. Moreover, the present findings demonstrated that Nab-paclitaxel and docetaxel exhibited a significantly increased pCR rate compared with that of paclitaxel liposomes in patients with HER2$^+$ and HR$^-$HER2$^-$ breast cancer. Consequently, patients with HER2$^+$ and HR$^-$HER2$^-$ breast cancer are potentially more suitable for NAC compared with those with HR$^+$HER2$^-$ breast cancer, especially the HR$^-$HER2$^+$ subgroup. The patients included in the present study were predominantly residents of the Jiangxi province, which may represent a limitation in regard to the generalization of the findings to a global population. Cancer cell differentiation degree may affect the pCR rate, however, not all of the

patients enrolled in the present study had differentiation data available from the pathology reports, particularly those with core needle biopsy samples; therefore, and differentiation data were not used to analyze separate subgroups. The HR status among the $HER2^+$ group were not further differentiated due to the low number of cases after subdivision. Furthermore, external validation of the predictive model was not conducted in the present study. The sensitivity and the specificity of the present model was 50.26 and 82.92% respectively, which indicated that the model exhibited a certain level of deficiency. Due to these limitations, further study regarding the different paclitaxel regimens effects on pCR rates are warranted in future.

In summary, the present study demonstrated that ER, PR and HER2 status, Ki-67 index and different types of taxanes are independent predictive factors for pCR in patients with breast cancer who receive NAC. Patients with ER^-, PR^-, $HER2^+$, Ki-67 index ≥30% breast cancer were more sensitive to NAC. Patients who received Nab-paclitaxel or docetaxel were more likely to achieve pCR compared with those who received paclitaxel liposomes, notably in the $HER2^+$ and HR^-HER2^- breast cancer subgroups. These findings indicated that molecular subtypes and taxane choice may significantly influence the likelihood of achieving pCR. Nab-paclitaxel and docetaxel were identified as effective taxanes, highlighting their potential clinical preference, especially in $HER2^+$ and HR^-HER2^- breast cancer.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

JD and YC contributed to the conception and design of the manuscript. JK, HX, XJ, ZH and YG were responsible for the acquisition, analysis and interpretation of data. XJ, YG and JD undertook the editing, drafting and writing of the manuscript. All authors confirm the authenticity of all the raw data, and read and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by the review board ethics committee of Nanchang People's Hospital (approval no. K-kt2024005; Nanchang, China). The requirement for patient approval or written informed consent was waived due to the retrospective nature of the study.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Han B, Zheng R, Zeng H, Wang S, Sun K, Chen R, Li L, Wei W and He J: Cancer incidence and mortality in China, 2022. J Natl Cancer Cent 4: 47-53, 2024.
2. Siegel RL, Giaquinto AN and Jemal A: Cancer statistics, 2024. CA Cancer J Clin 74: 12-49, 2024.
3. Li Y, Song W, Gao P, Guan X, Wang B, Zhang L, Yao Y, Guo Y, Wang Y, Jiang S and Sun S: Global, regional, and national burden of breast, cervical, uterine, and ovarian cancer and their risk factors among women from 1990 to 2021, and projections to 2050: Findings from the global burden of disease study 2021. BMC Cancer 25: 330, 2025.
4. Freitas AJA, Causin RL, Varuzza MB, Hidalgo Filho CMT, Silva VDD, Souza CP and Marques MMC: Molecular biomarkers predict pathological complete response of neoadjuvant chemotherapy in breast cancer patients: Review. Cancers (Basel) 13: 5477, 2021.
5. Dubsky P, Pinker K, Cardoso F, Montagna G, Ritter M, Denkert C, Rubio IT, de Azambuja E, Curigliano G, Gentilini O, *et al*: Breast conservation and axillary management after primary systemic therapy in patients with early-stage breast cancer: the Lucerne toolbox. Lancet Oncol 22: e18-e28, 2021.
6. Hurvitz SA, Martin M, Symmans WF, Jung KH, Huang CS, Thompson AM, Harbeck N, Valero V, Stroyakovskiy D, Wildiers H, *et al*: Neoadjuvant trastuzumab, pertuzumab, and chemotherapy versus trastuzumab emtansine plus pertuzumab in patients with HER2-positive breast cancer (KRISTINE): A randomised, open-label, multicentre, phase 3 trial. Lancet Oncol 19: 115-126, 2018.
7. Kim HJ, Dominici L, Rosenberg SM, Zheng Y, Pak LM, Poorvu PD, Ruddy KJ, Tamimi R, Schapira L, Come SE, *et al*: Surgical treatment after neoadjuvant systemic therapy in young women with breast cancer: Results from a prospective cohort study. Ann Surg 276: 173-179, 2022.
8. von Minckwitz G, Blohmer JU, Costa SD, Denkert C, Eidtmann H, Eiermann W, Gerber B, Hanusch C, Hilfrich J, Huober J, *et al*: Response-guided neoadjuvant chemotherapy for breast cancer. J Clin Oncol 31: 3623-3630, 2013.
9. Conforti F, Pala L, Sala I, Oriecuia C, De Pas T, Specchia C, Graffeo R, Pagan E, Queirolo P, Pennacchioli E, *et al*: Evaluation of pathological complete response as surrogate endpoint in neoadjuvant randomised clinical trials of early stage breast cancer: Systematic review and meta-analysis. BMJ 375: e066381, 2021.
10. de Azambuja E, Holmes AP, Piccart-Gebhart M, Holmes E, Di Cosimo S, Swaby RF, Untch M, Jackisch C, Lang I, Smith I, *et al*: Lapatinib with trastuzumab for HER2-positive early breast cancer (NeoALTTO): Survival outcomes of a randomised, open-label, multicentre, phase 3 trial and their association with pathological complete response. Lancet Oncol 15: 1137-1146, 2014.
11. Cortazar P, Zhang L, Untch M, Mehta K, Costantino JP, Wolmark N, Bonnefoi H, Cameron D, Gianni L, Valagussa P, *et al*: Pathological complete response and long-term clinical benefit in breast cancer: The CTNeoBC pooled analysis. Lancet 384: 164-172, 2014.
12. Zheng Q, Yan H, He Y, Wang J, Zhang N, Huo L, Liu Y, Wang L, Xu L and Fan Z: An ultrasound-based nomogram for predicting axillary node pathologic complete response after neoadjuvant chemotherapy in breast cancer: Modeling and external validation. Cancer 130: 1513-1523, 2024.
13. Değerli E, Şentürk Öztaş N, Alkan G, Bedir Ş, Derin S, Valıkhanova N, Saraç B, Kacar E, Demirci NS, Demirelli HF and Turna H: Relationship between pathological response and molecular subtypes in locally advanced breast cancer patients receiving neoadjuvant chemotherapy. J Chemother 35: 29-38, 2023.

14. Zhang T, Liu Y and Tian T: Predicting pathological complete response after neoadjuvant chemotherapy in breast cancer by clinicopathological indicators and ultrasound parameters using a nomogram. Sci Rep 14: 16348, 2024.
15. Sikov WM, Berry DA, Perou CM, Singh B, Cirrincione CT, Tolaney SM, Kuzma CS, Pluard TJ, Somlo G, Port ER, *et al*: Impact of the addition of carboplatin and/or bevacizumab to neoadjuvant once-per-week paclitaxel followed by dose-dense doxorubicin and cyclophosphamide on pathologic complete response rates in stage II to III triple-negative breast cancer: CALGB 40603 (Alliance). J Clin Oncol 33: 13-21, 2015.
16. Choi HJ, Ryu JM, Kim I, Nam SJ, Kim SW, Yu J, Lee JE and Lee SK: Nomogram for accurate prediction of breast and axillary pathologic response after neoadjuvant chemotherapy in node positive patients with breast cancer. Ann Surg Treat Res 96: 169-176, 2019.
17. Maimaitiaili A, Li Y, Chai N, Liu Z, Ling R, Zhao Y, Yang H, Liu Y, Liu K, Zhang J, *et al*: A nomogram for predicting pathologic node negativity after neoadjuvant chemotherapy in breast cancer patients: A nationwide, multicenter retrospective cohort study (CSBrS-012). Front Oncol 14: 1326385, 2024.
18. Anthracycline-containing and taxane-containing chemotherapy for early-stage operable breast cancer: A patient-level meta-analysis of 100 000 women from 86 randomised trials. Lancet 401: 1277-1292, 2023.
19. Nižnanský Ľ, Osinová D, Kuruc R, Hengerics Szabó A, Szórádová A, Masár M and Nižnanská Ž: Natural taxanes: From plant composition to human pharmacology and toxicity. Int J Mol Sci 23: 15619, 2022.
20. Gradishar WJ, Moran MS, Abraham J, Abramson V, Aft R, Agnese D, Allison KH, Anderson B, Bailey J, Burstein HJ, *et al*: Breast cancer, version 3.2024, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 22: 331-357, 2024.
21. Symons R, Heath F, Duggan J, Bui KT, Byun L, Friedlander M and Lee YC: Rates of paclitaxel hypersensitivity reactions using a modified Markman's infusion protocol as primary prophylaxis. Support Care Cancer 32: 292, 2024.
22. Bi Z, Chen P, Liu YB, Zhao T, Sun X, Song XR and Wang YS: Efficacy and safety analysis of paclitaxel, docetaxel and liposomal paclitaxel after neoadjuvant therapy in breast cancer. Breast Cancer Res Treat 184: 397-405, 2020.
23. Dieci MV, Griguolo G, Bottosso M, Tsvetkova V, Giorgi CA, Vernaci G, Michieletto S, Angelini S, Marchet A, Tasca G, *et al*: Impact of estrogen receptor levels on outcome in non-metastatic triple negative breast cancer patients treated with neoadjuvant/adjuvant chemotherapy. NPJ Breast Cancer 7: 101, 2021.
24. Giuliano AE, Edge SB and Hortobagyi GN: Eighth Edition of the AJCC cancer staging manual: Breast cancer. Ann Surg Oncol 25: 1783-1785, 2018.
25. Kerr AJ, Dodwell D, McGale P, Holt F, Duane F, Mannu G, Darby SC and Taylor CW: Adjuvant and neoadjuvant breast cancer treatments: A systematic review of their effects on mortality. Cancer Treat Rev 105: 102375, 2022.
26. Spring LM, Fell G, Arfe A, Sharma C, Greenup R, Reynolds KL, Smith BL, Alexander B, Moy B, Isakoff SJ, *et al*: Pathologic complete response after neoadjuvant chemotherapy and impact on breast cancer recurrence and survival: A comprehensive Meta-analysis. Clin Cancer Res 26: 2838-2848, 2020.
27. Ortmann O, Blohmer JU, Sibert NT, Brucker S, Janni W, Wöckel A, Scharl A, Dieng S, Ferencz J, Inwald EC, *et al*: Current clinical practice and outcome of neoadjuvant chemotherapy for early breast cancer: Analysis of individual data from 94,638 patients treated in 55 breast cancer centers. J Cancer Res Clin Oncol 149: 1195-1209, 2023.
28. Guan D, Jie Q, Wu Y, Xu Y, Hong W and Meng X: Real-world data on breast pathologic complete response and disease-free survival after neoadjuvant chemotherapy for hormone receptor-positive, human epidermal growth factor receptor-2-negative breast cancer: A multicenter, retrospective study in China. World J Surg Oncol 20: 326, 2022.
29. Villegas SL, Nekljudova V, Pfarr N, Engel J, Untch M, Schrodi S, Holms F, Ulmer HU, Fasching PA, Weber KE, *et al*: Therapy response and prognosis of patients with early breast cancer with low positivity for hormone receptors-An analysis of 2765 patients from neoadjuvant clinical trials. Eur J Cancer 148: 159-170, 2021.
30. Gianni L, Pienkowski T, Im YH, Roman L, Tseng LM, Liu MC, Lluch A, Staroslawska E, de la Haba-Rodriguez J, Im SA, *et al*: Efficacy and safety of neoadjuvant pertuzumab and trastuzumab in women with locally advanced, inflammatory, or early HER2-positive breast cancer (NeoSphere): A randomised multicentre, open-label, phase 2 trial. Lancet Oncol 13: 25-32, 2012.
31. Loibl S, O'Shaughnessy J, Untch M, Sikov WM, Rugo HS, McKee MD, Huober J, Golshan M, von Minckwitz G, Maag D, *et al*: Addition of the PARP inhibitor veliparib plus carboplatin or carboplatin alone to standard neoadjuvant chemotherapy in triple-negative breast cancer (BrighTNess): A randomised, phase 3 trial. Lancet Oncol 19: 497-509, 2018.
32. Nanda R, Liu MC, Yau C, Shatsky R, Pusztai L, Wallace A, Chien AJ, Forero-Torres A, Ellis E, Han H, *et al*: Effect of pembrolizumab plus neoadjuvant chemotherapy on pathologic complete response in women with early-stage breast cancer: An analysis of the ongoing phase 2 adaptively randomized I-SPY2 trial. JAMA Oncol 6: 676-684, 2020.
33. Schmid P, Cortes J, Pusztai L, McArthur H, Kümmel S, Bergh J, Denkert C, Park YH, Hui R, Harbeck N, *et al*: Pembrolizumab for early Triple-negative breast cancer. N Engl J Med 382: 810-821, 2020.
34. Dou H, Li F, Wang Y, Chen X, Yu P, Jia S, Ba Y, Luo D, Gao T, Li Z and Xiao M: Estrogen receptor-negative/progesterone receptor-positive breast cancer has distinct characteristics and pathologic complete response rate after neoadjuvant chemotherapy. Diagn Pathol 19: 5, 2024.
35. Ahn S, Woo JW, Lee K and Park SY: HER2 status in breast cancer: Changes in guidelines and complicating factors for interpretation. J Pathol Transl Med 54: 34-44, 2020.
36. Roskoski R Jr: The ErbB/HER family of protein-tyrosine kinases and cancer. Pharmacol Res 79: 34-74, 2014.
37. Baumgartner A, Tausch C, Hosch S, Papassotiropoulos B, Varga Z, Rageth C and Baege A: Ultrasound-based prediction of pathologic response to neoadjuvant chemotherapy in breast cancer patients. Breast 39: 19-23, 2018.
38. Denkert C, Loibl S, Müller BM, Eidtmann H, Schmitt WD, Eiermann W, Gerber B, Tesch H, Hilfrich J, Huober J, *et al*: Ki67 levels as predictive and prognostic parameters in pretherapeutic breast cancer core biopsies: A translational investigation in the neoadjuvant GeparTrio trial. Ann Oncol 24: 2786-2793, 2013.
39. Kim SY, Cho N, Choi Y, Lee SH, Ha SM, Kim ES, Chang JM and Moon WK: Factors affecting pathologic complete response following neoadjuvant chemotherapy in breast cancer: Development and validation of a predictive nomogram. Radiology 299: 290-300, 2021.
40. Li Y, Chen X, Zhu Q, Chen R, Xu L, Li S, Shi X, Xu H, Xu Y, Zhang W, *et al*: Retrospective comparisons of nanoparticle albumin-bound paclitaxel and docetaxel neoadjuvant regimens for breast cancer. Nanomedicine (Lond) 16: 391-400, 2021.
41. Wu X, Ye C, Wang X, Cai R, Yang J, Yu X, Zhou Y, Shen L, Zhu Y and Liu X: The efficacy and toxicity of neoadjuvant chemotherapy regimens of epirubicin plus cyclophosphamide followed by docetaxel or paclitaxel in female breast cancer patients. Cancer Manag Res 13: 1517-1527, 2021.
42. Jivani A and Shinde RK: A comprehensive review of taxane treatment in breast cancer: Clinical perspectives and toxicity profiles. Cureus 16: e59266, 2024.
43. Zhang W, Wang Y, He J, Xu Y, Chen R, Wan X, Shi W, Huang X, Xu L, Wang J and Zha X: Efficacy comparisons of solvent-based paclitaxel, liposomal paclitaxel, nanoparticle albumin-bound paclitaxel, and docetaxel after neoadjuvant systemic treatment in breast cancer. Nanomedicine 54: 102707, 2023.
44. Zhang W, Xu Y, Shi X, Huang X, Chen R, Xu H, Shi W, Wan X, Wang Y, He J, *et al*: Nanoparticle albumin-bound paclitaxel is superior to liposomal paclitaxel in the neoadjuvant treatment of breast cancer. Nanomedicine (Lond) 17: 683-694, 2022.