# Original Article

# Therapeutic effects of epirubicin combined with capecitabine for patients with triple negative breast cancer

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Abstract: Objective: The aim of the current study was to explore the therapeutic effects of epirubicin combined with capecitabine for patients with triple negative breast cancer (TNBC). Methods: A total of 80 patients with TNBC were enrolled and divided into the control group and observation group, according to a random number table. Expression levels of carcinoembryonic antigen (CEA) and neutrophil lymphocyte ratio (NLR) in the two groups were observed before and after treatment. Adverse conditions of the two groups were also observed. The patients were grouped according to clinical efficacy after treatment. Five-year overall survival curves were drawn and Cox's regression analysis was used to analyze independent prognostic factors. Results: Clinical efficacy levels of the observation group were better than those of the control group (P < 0.05). Improvement levels in the observation group, after treatment, were greater than those in the control group (P < 0.05). Differences in expression levels of CEA and NLR in the observation group were higher than those in the control group (P < 0.05). Expression levels of CEA and NLR in the group with good efficacy before treatment were lower than those in the group with poor efficacy (P < 0.05). Fiveyear survival rates of patients with low CEA and NLR expression levels were higher than those of patients with high expression (P = 0.022, P = 0.040). Multivariate regression analysis showed that clinical staging was an independent prognostic factor affecting the survival of TNBC patients. Conclusion: Epirubicin combined with capecitabine can effectively improve clinical treatment efficacy levels of TNBC patients. Expression levels of CEA and NLR, before and after treatment, can be used as outcome measures for survival and prognosis.

Keywords: Epirubicin, capecitabine, triple negative breast cancer, CEA

#### Introduction

Breast cancer is the most common malignant tumor in women. According to worldwide cancer statistics, there were 2.089 million new female patients with breast cancer in the world in 2018, accounting for 24.22% of all female cancer incidence. Deaths of female patients with breast cancer have risen to 626,700, accounting for 15.03% of all female cancer mortality [1]. High incidence and mortality rates pose a great threat to the quality of life, health, and safety of women. Breast cancer is a highly heterogeneous malignant tumor [2]. Triple negative breast cancer (TNBC) is the most dangerous subtype of breast cancer. TNBC is a kind of breast cancer with a negative estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (Her-2), accounting for 15%-20% of breast cancer cases. Incidence of TNBC is relatively insidious. However, once the disease occurs, it is more serious, aggressive, and prone to recurrence. Clinical prognosis is not ideal. It is insensitive to endocrine therapy. Moreover, it lacks effective molecular target gene therapy drugs [3]. Therefore, patient conditions can only be controlled by chemotherapy [4].

Anthracyclines are important chemotherapeutic drugs for breast cancer patients. Epirubicin, an anthracycline drug, is directly embedded in DNA base pairs, aiming to interfere with the transcription process. This inhibits the formation of mRNA [5]. In addition, it provides inhibition effects on topoisomerase II, inhibiting the growth and metastasis of tumors [6]. Capecitabine is a new drug for selective targeting therapy of cancer. It can be absorbed completely in the digestive tract by oral administra-

tion, promoting the transformation of fluorouracil and killing tumor cells, with less damage to the body [7]. Previous studies have shown that both drugs can markedly improve TNBC conditions [8]. After treatment, conditions of the patients were assessed according to changes in primary lesions and different metastasis sites.

However, there are no relevant studies concerning whether conditions of patients can be predicted by observing relevant indicators before treatment. Carcinoembryonic antigen (CEA) is the most common clinical diagnostic marker of tumors. It changes during the course of tumorigenesis [9]. Neutrophil lymphocyte ratio (NLR) is a popular inflammatory marker used in recent years. Due to abnormalities of leukocyte subsets in patients with tumors, expression of NLR is different [10]. Current studies have shown that expression of NLR is closely related to the prognosis of patients with hepatocellular carcinoma. However, there are few studies concerning TNBC [11].

The current study observed changes in CEA and NLR expression in TNBC patients, before and after treatment, investigating the predictive value of the therapeutic effects of the two indicators in TNBC. Epirubicin combined with capecitabine can effectively improve clinical treatment efficacy levels have of TNBC patients.

#### Materials and methods

#### Clinical data

The present study selected 80 patients with TNBC, treated in Dong E Hospital, from January 2013 to March 2014. According to a random number table, they were divided into the control group (n = 40), treated with epirubicin alone, and the observation group (n = 40), treated with epirubicin combined with capecitabine. Patients in the control group and observation group were aged  $48.2 \pm 7.2$  years old and  $49.0 \pm 6.2$  years, respectively. The current study was approved by Medical Ethics Committee of Dong E Hospital.

Inclusion criteria: Patients were diagnosed with TNBC by pathological and immunohistochemical tests (ER, PR, and Her-2 were negative); Lesions of the patients could be measured and the expected survival time was more than 3 months. Exclusion criteria: Patients with congenital heart, kidney, liver, and lung dysfunc-

tion; Patients with immunodeficiency disorders, severe infections, and trauma before treatment; Patients with other malignant tumors; Patients with incomplete clinical data; Patients that did not cooperate with treatment.

#### Drug sources

Epirubicin hydrochloride for injection (Zhejiang Haizheng Pharmaceutical Co., Ltd., China, State Medical Permitment: H20041211); Capecitabine (Shanghai Roche Pharmaceutical Co., Ltd., China, State Medical Permitment: H20073024).

#### Therapeutic regimen

Patients in the control group were treated with epirubicin hydrochloride for injection: Epirubicin  $60~\text{mg/m}^2$  and 0.9% normal saline 100~mL were given through intravenous drip, once per day, for a total of 21 days (a course of treatment). Patients in the observation group were treated with capecitabine, as follows: Capecitabine 1,250  $\text{mg/m}^2$  via oral administration, b.i.d, starting from day 1, for a total of 14 days, with 21 days as a course of treatment. Patients in the two groups were treated with 4 courses.

#### Follow-ups

Survival follow-ups were performed by telephone and outpatient reviews. Follow-ups were conducted every 3 months in the first year after treatment and every 6 months thereafter. Follow-ups lasted for 5 years.

# Detection of CEA and NLR

Six mL peripheral blood samples were collected before treatment (the day before chemotherapy) and after treatment (4 courses). They were sent to the Department of Laboratory for detection. CEA was detected by ADVIA Centaur CP (Siemens, Germany), while NLR was detected by XS-500i automatic blood analyzer (Sysmex, Japan).

#### Outcome measures

Main outcome measures: Clinical efficacy levels of patients in the two groups, after treatment, were observed. Expression levels of CEA and NLR in the two groups, before and after treatment, were observed. Adverse reactions of patients during the treatment courses were

observed (patients were given appropriate treatment as adverse reactions occurred and drug withdrawal was conducted if the situation worsened). According to clinical efficacy, expression levels of CEA and NLR, before treatment, in the groups with good efficacy and poor efficacy were observed. The predictive value of the two indicators on clinical efficacy levels of patients was analyzed using receiver operating characteristic (ROC) curves.

Secondary outcome measures: Clinical data of the control group and observation group was compared. According to the median of CEA and NLR, after treatment, the patients were divided into high and low expression groups. Five-year overall survival curves were drawn and Cox's regression analysis was used to analyze independent prognostic factors.

Efficacy evaluation criteria: According to efficacy criteria of solid tumors, recent clinical efficacy levels of patients were evaluated. They were divided into four levels, including complete remission (CR), partial remission (PR), stable disease (SD), and progressive disease (PD). CR: After treatment, lesions disappeared completely and the disappearance time lasted for more than 4 weeks; PR: After treatment, the total maximum diameter of the lesions was decreased by more than 50%; SD: After treatment, the total maximum diameter of the lesions was decreased by less than 50%; PD: After treatment, the total maximum diameter of the lesions was decreased by more than 25% or there were new lesions.

#### Statistical analysis

SPSS20.0 software was used for statistical analysis. GraphPad 7 software was used to draw required pictures. K-S tests were used to analyze the distribution of dose data. Normal distribution data are expressed by mean ± standard deviation (Mean ± SD). Independent sample t-tests were used for comparisons between the two groups, while paired t-tests were used for comparisons within the group. Data that did not conform to normal distribution are expressed by quartiles [Means (P25-P75)] and were analyzed by non-parametric tests, expressed by Z. Enumeration data are expressed by rates (%) and were analyzed by Chi-square tests, expressed by X2, Fisher's test was used when theoretical number T < 1 or n < 40. Ranked data was analyzed by rank-sum

tests, expressed by Z. ROC was used to draw the predictive value of CEA and NLR on clinical efficacy levels of patients. K-M survival curves were used to draw the survival of patients and log-rank testing was used to analyze patient 5-year survival rates. Multivariate regression was used to analyze independent risk factors affecting the prognosis of patients. P < 0.05 indicates statistical differences.

#### Results

#### Comparison of clinical data

Comparing the clinical data of the two groups, there were no differences in age, BMI, past medical history, smoking history, family history, tumor size, clinical staging, and pathological type between the control group and observation group (P > 0.05) (Table 1).

### Clinical efficacy

According to efficacy criteria of solid tumors, clinical efficacy levels of patients were evaluated after treatment. Results showed that there were 10 cases of CR, 13 cases of PR, 12 cases of SD, and 5 cases of PD in the control group. There were 16 cases of CR, 15 cases of PR, 8 cases of SD, and 1 case of PD in the observation group. There were significant differences in clinical efficacy comparisons of CR+PR between the two groups of patients (P < 0.05) (Table 2).

Expression of CEA and NLR in the two groups after treatment

There were no differences in expression of CEA and NLR between the two groups before treatment (P > 0.05). After treatment, expression of CEA and NLR in the two groups was markedly improved. Improvement levels in the observation group were greater than those in the control group (P < 0.05). Differences in expression levels of CEA and NLR in the observation group were higher than those in the control group (P < 0.05) (Table 3).

# Adverse reactions during treatment

Adverse reactions of the two groups were effectively improved after corresponding treatment. No patients stopped taking medicine for treatment. Adverse reactions in the two groups, during treatment, were statistically analyzed. In the control group, there was 1 case of cardiac damage, 3 cases of neutrophil decrease, 2 cases of liver damage, and 3 cases of gastroin-

Table 1. Clinical data of patients

Factor	Control group (n = 40)	Observation group (n = 40)	t/X <sup>2</sup> /Z value	P value
Age (years)	48.2 ± 7.2	49.0 ± 6.2	0.533	0.596
BMI (kg/m²)	22.14 ± 2.12	22.35 ± 1.92	0.464	0.644
Anamnesis				
Hypertension	15 (37.50)	11 (27.50)	0.912	0.34
Diabetes mellitus	9 (22.50)	11 (27.50)	0.267	0.606
Hyperlipemia	10 (25.00)	7 (17.50)	0.672	0.412
Smoking history			0.672	0.412
Yes	10 (25.00)	7 (17.50)		
No	30 (75.00)	33 (82.50)		
Family history			0.621	0.431
Yes	8 (20.00)	11 (27.50)		
No	32 (80.00)	29 (72.50)		
Tumor size			1.125	0.263
≤ 5 cm	22 (55.00)	17 (42.50)		
> 5 cm	18 (45.00)	23 (57.50)		
Clinical staging			-1.067	0.286
II stages	10 (25.00)	14 (35.00)		
III stages	24 (60.00)	22 (55.00)		
IV stages	6 (15.00)	4 (10.0)		
Pathological type			0.386	0.943
Adenocarcinoma	5 (12.50)	5 (12.50)		
Cephaloma	7 (17.50)	6 (15.00)		
Mucinous adenocarcinoma	6 (15.00)	8 (20.00)		
Invasive ductal carcinoma	22 (55.00)	21 (52.50)		

Note: BMI: body mass index.

**Table 2.** Comparison of clinical efficacy between the two groups of patients

Group	CR	PR	SD	PD	Z value	P value
Control group (n = 40)	10 (25.00)	13 (32.50)	12 (30.00)	5 (12.50)	-2.051	0.040
Observation group $(n = 40)$	16 (40.00)	15 (37.5)	8 (20.00)	1 (2.50)		

Table 3. Changes in CEA and NLR in the observation group and control group

Group		CEA (µg/mL)		NLR			
	Pretherapy	Post-treatment	D-value	Pretherapy	Post-treatment	D-value	
Control group (n = 40)	13.24 ± 4.93	8.33 ± 3.04	4.90 ± 2.06	3.10 ± 0.71	2.61 ± 0.75	0.48 ± 0.28	
Observation group (n = 40)	13.74 ± 3.76	6.45 ± 2.75	7.28 ± 3.25	3.26 ± 0.66	2.24 ± 0.62	1.02 ± 0.58	
t value	0.610	2.901	3.912	1.044	2.405	5.303	
P value	0.612	0.005	< 0.001	0.300	0.019	< 0.001	

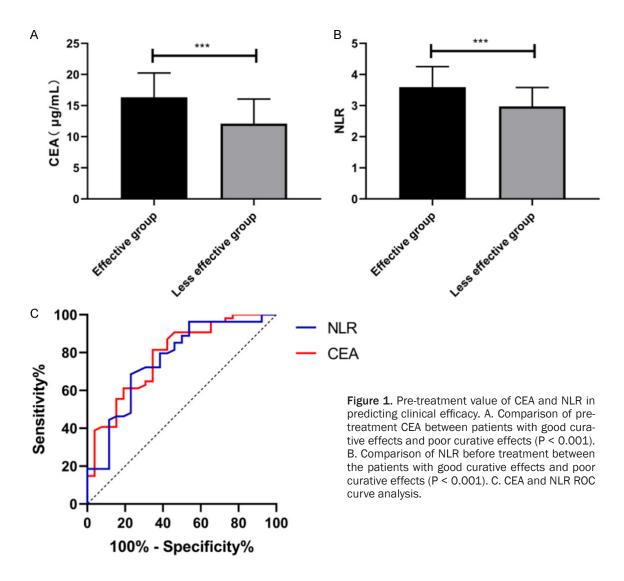
testinal reaction. In the observation group, there was 1 case of cardiac damage, 2 cases of neutrophil decrease, 1 case of liver damage, and 1 case of gastrointestinal reaction. There were no differences in incidence of adverse reactions between the two groups (P > 0.05) (Table 4).

Predictive value of pre-treatment CEA and NLR on clinical efficacy

According to the clinical efficacy of 80 patients after treatment, CR+PR patients were assigned to the good efficacy group (n = 54). SD+PD patients were assigned to the poor efficacy

**Table 4.** Incidence of adverse reactions in patients

Group	Cardiac damage patient number (%)	Neutrophil decrease patient number (%)	Liver damage patient number (%)	Gastrointestinal reaction patient number (%)	Total incidence patient number (%)
Control group (n = 40)	1 (2.50)	3 (7.50)	2 (5.00)	3 (7.50)	9 (22.50)
Observation group (n = 40)	1 (2.50)	2 (5.00)	1 (2.50)	1 (2.50)	5 (12.50)
X <sup>2</sup>					1.385
P value	> 0.999	> 0.999	> 0.999	0.615	0.239



group (n = 26). Comparing CEA and NLR levels of the two groups before treatment, it was found that expression levels of pre-treatment CEA and NLR in the good efficacy group were lower than those in the poor efficacy group (P < 0.05) (**Figure 1A** and **1B**). ROC curves of pre-treatment CEA and NLR expression levels were drawn to analyze their predictive value for clinical efficacy. Results showed that the AUC of CEA and NLR was 0.784 and 0.760. The

95 Cl% was 0.676-0.892 and 0.643-0.877, respectively (**Table 5** and **Figure 1C**).

Relationship between CEA, NLR, and 5-year survival of TNBC after treatment

The 5-year survival of 80 patients was 61.25% (Figure 2A-C). According to the median of CEA and NLR, after treatment, the patients were divided into high and low expression

Table 5. ROC parameters

Factor	AUC	95% CI	Specificity	Sensitivity	Youden index	Cut-off
CEA	0.784	0.676~0.892	65.38%	81.48%	46.86%	< 14.920
NLR	0.760	0.643~0.877	76.92%	68.52%	45.44%	< 3.255

Note: area under curve (AUC), confidence interval (95% CI), optimal cut-off value (Cut-off).

groups. The 5-year survival of patients with low CEA and NLR expression was higher than that of patients with high expression ( $P_{CEA} = 0.022$ ,  $P_{NLR} = 0.040$ ).

#### Cox regression analysis

Patient data was collected for univariate Cox regression analysis. Results showed that tumor size, clinical staging, CEA, and NLR were all prognostic factors affecting the survival of TNBC patients. Subsequently, multivariate Cox regression analysis was used for meaningful single-factor indicators. Results revealed that clinical staging (HR: 9.754, 95 CI%: 4.273-22.266), CEA (HR: 5.844, 95 CI%: 1.943-17.578), and NLR (HR: 4.085, 95 CI%: 1.559-10.707) were independent prognostic factors affecting the survival of TNBC patients (**Tables 6-8**).

#### Discussion

Breast cancer is currently the top ranked malignant tumor endangering the health of women, worldwide. It is a highly heterogeneous malignant tumor. In a study by DeSantis [12], 231,840 new invasive breast cancer patients and 40,290 deaths were reported in the United States in 2015. One of the subtypes of breast cancer, TNBC accounts for about 15% of all breast cancer cases [13]. As ER, PR, and Her-2 are negative, these patients cannot receive endocrine and targeted therapy. Moreover, the clinical prognosis is not ideal. At present, there are no unified therapeutic regimens for TNBC. Thus, clinicians mainly use conventional chemotherapy [14].

Epirubicin, a chemotherapeutic drug with a high usage rate in the treatment of breast cancer, can interfere with the synthesis of DNA and RNA in cancer cells by directly embedding DNA bases. It can also regulate levels of active oxygen by inhibiting the activity of topoisomerase II, killing cancer cells through various pathways [15]. Capecitabine, a new type of targeted anti-

tumor drug, can be converted from fluoropyrimidine carbamate to 5-fluorouracil. The concentration of capecitabine in tumor tissues is higher than that in normal tissues. Capecitabine can be

used for a long time without precipitation accumulation in patients [16]. In this study, the effects of epirubicin combined with capecitabine on clinical efficacy levels of TNBC patients were compared. Results showed that clinical efficacy levels of the observation group were better than those of the control group after treatment, indicating that combined treatment could improve patient conditions better than singular treatment. In Ye's [17] study, the efficacy of epirubicin combined with capecitabine for treatment of TNBC was higher than that in the single treatment. In addition, effective rates of single treatment (57.50%) and combined treatment (77.50%) were slightly higher than those in Ye's study. It was speculated that Ye's study samples were all TNBC patients in stages III and IV, while stage II patients were included in the present study. Earlier treatment generally leads to better efficacy. This may be one of the reasons for the higher effective rate of the present study. In the course of chemotherapy, there will be different degrees of adverse reactions. These are due to the different physical conditions of patients. According to statistics, there was cardiac damage, neutrophil decrease, liver damage, and gastrointestinal reactions in both groups. However, there were no differences in total incidence of adverse reactions between the two groups. This suggests that combined treatment did not increase adverse reactions of patients and could effectively improve clinical efficacy levels of patients. Thus, it is suitable for clinical promotion.

At present, clinical efficacy evaluations of tumor patients are mainly based on the efficacy criteria of solid tumors. This further evaluates the clinical efficacy of patients using image detection of changes in tumor size. However, image detection has a certain impact on human health. Can we observe the clinical efficacy of patients using relevant serum indexes? Expression levels of CEA and NLR were also detected before and after treatment. CEA, an

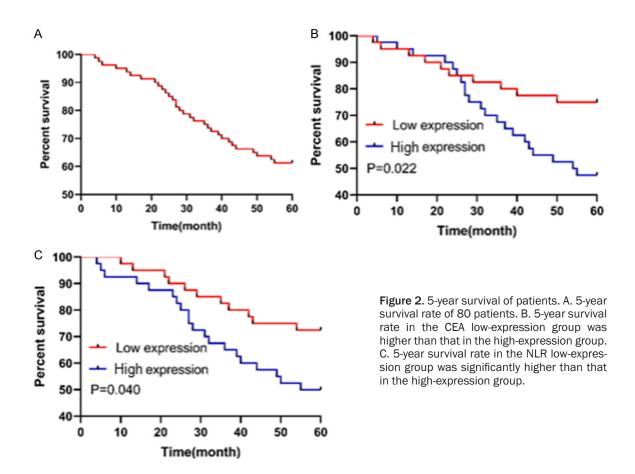


Table 6. Assignment table

Factor	Assignment
Age	< 50 = 1, ≥ 50 = 2
BMI	$< 22 \text{ kg/m}^2 = 1, \ge 22 \text{ kg/m}^2 = 2$
High blood pressure	Yes = $1$ , No = $2$
Diabetes	Yes = 1, No = 2
Hyperlipidemia	Yes = 1, No = 2
Smoking history	Yes = 1, No = 2
Family history	Yes = 1, No = 2
Tumor size	$\leq$ 5 cm = 1, > 5 cm = 2
Clinical stages	II stages = 1, III stages = 2, IV stages = 3
Pathological type	Invasive ductal carcinoma = 1, others = 2
CEA	< 7.46 $\mu$ g/mL = 1, $\geq$ 7.46 $\mu$ g/mL = 2 (7.46 is the mean value of patients after treatment)
NLR	< 2.44 = 1, Sup2.44 = 2 (2.44 is the mean after the patient's treatment)
Survival state	Death = 1, Survival = 2
Survival time	Continuous variables using raw data analysis

acid glycoprotein, has immunosuppressive effects. Expression of CEA is increased with occurrence and development of tumors. Previous studies have shown that expression levels of CEA in serum of TNBC patients were markedly increased [18, 19]. NLR is the neutro-

phil-to-lymphocyte ratio. Some studies have shown that expression of leukocyte subsets is abnormal in cancer patients [20], while other studies [21] have shown that NLR is closely related to the prognosis of patients after radical surgery. Observing expression levels of CEA

Table 7. Single factor Cox regression

Footor	D	SE	Wald	Sig.	Exp (β)	95% CI f	or Exp (β)
Factor	β	- SE				Low	Up
Age	-0.735	0.411	3.196	0.074	0.480	0.214	1.073
BMI	-0.094	0.361	0.068	0.795	0.910	0.449	1.847
High blood pressure	-0.171	0.376	0.208	0.648	0.843	0.403	1.760
Diabetes	0.232	0.430	0.291	0.590	1.261	0.543	2.927
Hyperlipidemia	-0.144	0.430	0.113	0.737	0.866	0.373	2.009
Smoking history	-0.224	0.430	0.270	0.603	0.800	0.344	1.857
Family history	-0.219	0.430	0.259	0.611	0.804	0.346	1.865
Tumor size	1.449	0.456	10.085	0.001	4.259	1.741	10.414
Clinical stages	2.661	0.384	47.968	0.000	14.310	6.739	30.386
Pathological type	0.413	0.375	1.208	0.272	1.511	0.724	3.154
CEA	2.249	0.492	20.897	0.000	9.481	3.614	24.87
NLR	1.878	0.457	16.903	0.000	6.543	2.672	16.02

Note: xt = General coefficient, SD = standard deviation, Wald = Chi-square value, Sig = test value, Exp(%) = HR, 95% CI = HR confidence interval.

Table 8. Multifactor Cox

Factor	β	SE	Wald	Sig.	Exp (β)	95% CI for Exp (β) Low Up		
						Low	Up	
Tumor size	0.230	0.529	0.189	0.664	1.258	0.446	3.549	
Clinical score stages	2.278	0.421	29.252	0.000	9.754	4.273	22.266	
CEA	1.765	0.562	9.871	0.002	5.844	1.943	17.578	
NLR	1.407	0.492	8.195	0.004	4.085	1.559	10.707	

Note: xt = General coefficient, SD = standard deviation, Wald = Chi-square value, Sig = test value, Exp(%) = HR, 95% CI = HR confidence interval.

and NLR, before and after treatment, in the control group and observation group, results suggest that expression levels of CEA and NLR in TNBC patients after treatment were decreased. The decreasing degree of the two indicators in combined treatment was higher than that in single treatment. In a report by Dai et al. [22], expression of CEA in TNBC patients after treatment was lower than that before treatment. In a study by Asano et al. [23], expression of NLR in TNBC patients after treatment was decreased. Remission of patients whose NLR was lower than 3.0 was better, indicating that the two indicators could be used as outcome measures of efficacy levels of TNBC. However, whether expression levels of CEA and NLR before treatment can be used to predict the clinical efficacy of patients has not yet been reported. Therefore, according to clinical efficacy levels of the patients after treatment, all patients were re-grouped. Expression levels of CEA and NLR, before treatment, in the good efficacy group were lower than those in the

efficacy group. The two indicators, before treatment, are expected to be used as predictive indicators of clinical efficacy levels of patients. Based on the data of two groups, ROC curves were drawn. Results showed that the AUC of the two indicators was larger than 0.7. Higher sensitivity and specificity levels were good predictive indicators. It was speculated that the two indicators can be used as outcome measures for predicting therapeutic effects, which may be related to the severity of patient conditions. However, the specific mechanisms are unclear, requiring further research.

Five-year follow-ups showed that the overall

5-year survival rate of the 80 patients was 61.25%, in accord with foreign literature [22]. Subsequently, the patients were divided into high and low expression groups, according to the median of CEA and NLR after treatment. It was found that the 5-year survival rate of patients with low expression of CEA and NLR was higher than that of patients with high expression, according to analysis via K-M survival curves. In Asano's study [23], the survival of patients with low NLR expression levels also increased significantly, in accord with present results. Li et al. [24] found that DFS (diseasefree survival) and OS (overall survival) rates of breast cancer patients with high CEA expression levels were lower than those of patients with low CEA expression, according to metaanalysis. It can be concluded that CEA and NLR can be used as survival predictive indicators of TNBC. However, whether CEA and NLR can be used as independent prognostic factors of TNBC remains unclear. Cox's regression analysis showed that clinical staging, CEA, and NLR are independent prognostic factors. Previous studies have shown that clinical staging is an independent prognostic factor of TNBC, with higher staging indicating the greater the risk of death [25]. In Shao's [26] study, CEA was shown to be an independent prognostic factor of TNBC. However, in a study by Asano et al. [23], NLR could not be used as an independent prognostic factor of TNBC, inconsistent with present results. The first reason is that there are differences in the process of sample classification and assignment. The second reason is that there are differences among samples. Clinical staging of the patients in the current study included mainly stage II-IV patients.

The current study confirmed the clinical efficacy of epirubicin combined with capecitabine in the treatment of TNBC. Expression levels of CEA and NLR, before treatment, were observed to predict clinical efficacy levels of patients. Expression levels of CEA and NLR, after treatment, may be used as independent prognostic indicators, evaluating the prognosis of patients. However, the present study had some limitations. First, this study did not further explore why pre-treatment CEA and NLR levels could be used as predictive indicators of therapeutic efficacy. Moreover, relevant mechanisms were not explored. Second, it was not clear whether the two indicators can be used as outcome measures of DFS. Therefore, future cross-sectional experiments should be conducted to further explore relevant mechanisms.

In conclusion, epirubicin combined with capecitabine can effectively improve clinical efficacy levels of TNBC patients. Moreover, expression levels of CEA and NLR, before and after treatment, can be used as outcome measures of clinical efficacy, survival, and prognosis.

#### Disclosure of conflict of interest

None.

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