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Does concomitant ductal carcinoma in situ influence the prognostic outcome after neoadjuvant therapy in triple-negative invasive ductal carcinoma?

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Abstract

Purpose Ductal carcinoma in situ (DCIS) is considered a precursor to invasive ductal carcinoma (IDC), and the coexistence of DCIS with IDC is often observed during the diagnosis of breast cancer. The aim of study is to investigated the clinicopathological features and prognosis of triple-negative IDC with DCIS following neoadjuvant therapy (NAT). Additionally, we explored the risk factors for residual DCIS in these patients post-NAT.

Methods This study included patients with stages II-III triple-negative breast cancer with histologically confirmed IDC who underwent radical surgery after NAT between January 2011 and December 2021. Baseline data, clinical features, pathological outcomes, and prognostic information were collected and analyzed.

Results A total of 315 patients were enrolled and categorized into the IDC + DCIS ($n = 67$) and IDC groups ($n = 248$) according to the composition of the pre-NAT biopsy. The proportion of patients with histological grade G3 (78.2% vs. 61.2%, $p = 0.004$) and a Ki-67 index > 20% (98.4% vs. 86.6%, $p < 0.001$) was significantly higher in the IDC group than in the IDC + DCIS group. Although no significant difference was observed in the 5-year overall survival (OS) (93.4% vs. 90.8%, $p = 0.298$) between the two groups, the 5-year disease-free survival (DFS) (90.6% vs. 83.5%, $p = 0.041$) of the IDC + DCIS group was significantly better than that in the IDC group. Multivariate analysis demonstrated that IDC + DCIS (HR: 0.502; 95% CI, 0.284–0.952; $p = 0.048$) was an independent prognostic factor for DFS. In addition, the clinical T3–T4 stage (OR = 3.891; 95% CI, 1.320–15.219, $p = 0.040$) and clinical N1–N3 (OR = 4.500; 95% CI, 1.495–13.564, $p = 0.012$) were independent preoperative predictors of residual DCIS after NAT in patients with IDC and DCIS components.

Conclusion The presence of DCIS component in patients with triple-negative IDC is associated with lower tumor aggressiveness and improved DFS after NAT compared to patients without DCIS. Additionally, clinical T and N stages are risk factors for residual DCIS after NAT in patients with triple-negative IDC and a DCIS component.

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Keywords Triple-negative breast cancer, Ductal carcinoma in situ, Invasive breast cancer, Neoadjuvant chemotherapy, Clinicopathological characteristics, Prognosis

Triple-negative breast cancer (TNBC) is a distinct molecular type of breast cancer, characterized by the absence of estrogen receptors (ER), progesterone receptors (PR), and human epidermal growth factor receptor 2 (HER2) expression. Patients with TNBC often have high tumor invasiveness, limited treatment options, and poor prognosis [1–3]. In recent years, neoadjuvant therapy (NAT) has been widely used in early-stage TNBC, offering several therapeutic advantages, including tumor burden reduction, increased breast-conservation surgery (BCS) rates, improved prognosis, and rapid drug evaluation effect [4, 5]. Previous studies have reported that invasive ductal carcinoma (IDC) may arise from pre-existing ductal carcinoma in situ (DCIS), with patients with IDC often presenting a DCIS component in preoperative biopsy [6]. However, IDC with DCIS tends to be less responsive to NAT, resulting in a higher probability of residual tumors after NAT. The extensive presence of DCIS is considered a key factor influencing the feasibility of BCS [7–9]. Given that the specificity and sensitivity of radiological features (such as calcifications or enhancement) in identifying residual DCIS remain unsatisfactory, it is necessary to explore the risk factors of residual DCIS after NAT in patients with IDC and a DCIS component in biopsy [10]. Moreover, a delay in the progression from DCIS to invasive form is believed to account for tumors with coexisting DCIS exhibiting lesser biological aggressiveness, such as earlier tumor stage, lower tumor grade, and reduced likelihood of lymph node invasion [10, 11]. However, triple-negative IDC less commonly coexisted with DCIS, and the prognosis of patients with triple-negative IDC with DCIS, particularly those undergoing NAT, remains controversial. Therefore, this study explored the clinicopathological features and prognosis of triple-negative IDC with DCIS following NAT, and the risk factors for residual DCIS in these patients post-NAT.

Materials and methods

This retrospective analysis was based on a breast cancer database with an inclusion period from January 2011 to December 2021. This database comprises patients who were diagnosed with breast cancer and underwent radical surgery at Peking University First Hospital and the Hebei Provincial Hospital of Traditional Chinese Medicine. The inclusion criteria were as follows: (1) triple-negative IDC confirmed by pre-NAT biopsy. (2) NAT administered for at least four cycles; and (3) clinical stages II–III. The exclusion criteria were as follows: (1) incomplete data; (2) distant metastasis; (3) previously diagnosed with other malignancies; and (4) occult, bilateral, or inflammatory breast cancer. The study was approved by the institutional ethics review committees of the two hospitals, and all enrolled patients provided signed informed consent.

Pathological evaluation criteria

The data collected were extracted from institutional databases and included clinical baseline characteristics, clinicopathological features, surgical procedures, and prognostic information. Pathological reports of pre-NAT biopsy and postoperative specimens were independently reviewed by experienced pathologists. The presence of a DCIS component was evaluated using pre-NAT biopsy and postoperative specimens per patient. The tumor grade, Ki-67 index, and receptor status were evaluated for IDC before NAT, but not for DCIS. A proportion of positive cells < 1% was defined as negative for ER and PR. HER2 status was defined as HER2-negative for scores of 0 or 1+, or HER2 2+/fluorescent in situ hybridisation (FISH)-negative. TNBC was defined as the absence of ER, PR, and HER2 expression. The positive rate of tumor cell nucleus cells ≥ 20% was defined as high expression of the Ki-67 index. According to the Nottingham grading system, the histological grading system of IDC can be divided into low (G1 level), intermediate (G2 level) and high (G3 level). The TNM classification is reported based on the eighth edition of the American Joint Committee on Cancer (AJCC) ([12]. Pathological complete response (pCR) is defined as the absence of invasive carcinoma components in breast lesions and axillary lymph nodes; however, the presence of residual DCIS components is allowed (ypT0/is N0) ([13].

Treatment strategies

NAT regimens were determined based on the guidelines of the Chinese Society of Clinical Oncology (CSCO) ([13] and recommendations from the multidisciplinary tumor board. NAT is mainly chemotherapy, and the use of taxanes combined with anthracycline cytotoxic drugs is greater than or equal to four cycles (docetaxel 75 mg/m^2 or albumin taxol 125 mg/m^2 d1 and d8 combined with pirarubicin 50 mg/m^2). In addition, some patients received immunotherapy (PD-1/PD-L1 inhibitors) combined with chemotherapy at the NAT stage, and immunotherapy drugs mainly included pembrolizumab, nivolumab, and sintilimab. After completion of NAT, radical surgery-either BCS or mastectomy-was performed. Sentinel lymph node biopsy (SLNB) was also performed on clinically node-negative patients before NAT, while axillary lymph node dissection (ALND) was performed

for clinically node-positive patients or those with positive SLNB results.

Statistical analysis

The data in this study were analyzed using SPSS software (version 26.0). Differences in continuous variables between the two groups were compared using the *t*-test, and the chi-square test was used to compare categorical variables between the two groups. Univariate logistic regression analysis was performed to evaluate the association between residual DCIS and variables. Variables with $p < 0.10$ in univariate analysis were included in the multivariate logistic regression model, and odds ratios (OR) and 95% confidence intervals (95% CIs) were used to examine the independent predictors of residual DCIS after NAT. The endpoints of this study were 5-year overall survival (OS) and 5-year disease-free survival (DFS). The survival curve was drawn using GraphPadPrism9.0 software and analyzed using the Kaplan–Meier method, and the survival difference between the groups was calculated using the log-rank test. Univariate analysis was conducted to identify the variables associated with OS and DFS. DCIS in pre-NAT biopsy and variables with *p*-value < 0.1 were included in multivariate Cox regression analysis to determine the hazard ratio (HR), 95%CI, and independent risk factors associated with survival. A *p* value < 0.05 was considered statistically significant.

Results

Clinical and pathological characteristics

A total of 315 patients with TNBC who underwent radical surgery after NAT from January 2013 to December 2021 were included in this study. All enrolled patients were categorized into the IDC + DCIS group ($n = 67$) and IDC group ($n = 248$) according to the composition of the pre-NAT biopsy. The clinical features, pathological characteristics, and prognostic outcomes of the two groups were compared and analyzed (Fig. 1).

The clinicopathological characteristics and analyses of the two groups are listed in Table 1. The proportion of patients with histological grade G3 (78.2% vs. 61.2%, $p = 0.004$) and Ki-67 index > 20% (98.4% vs. 86.6%, $p < 0.001$) was significantly higher in the IDC group than in the IDC + DCIS group. Additionally, compared with patients in the IDC group, those in the IDC + DCIS group were more likely to have DCIS residues after NAT (56.7% vs. 24.2%, $p < 0.001$). No significant differences were observed in age, family history of breast cancer, neoadjuvant immunotherapy, tumor location, clinical T stage, clinical nodal status, type of surgery, pCR, or adjuvant radiotherapy between the two groups ($p > 0.05$).

Survival outcomes

The follow-up deadline was December 2023, with a mean follow-up of 63 months (min, 14 months; max, 155 months). A total of 46 patients experienced endpoint events related to recurrence or distant metastasis, and 21 died. The Kaplan–Meier method was used to analyze the survival outcomes. The results demonstrated no significant difference in OS between the IDC + DCIS and IDC groups, with both groups having a 5-year OS of 93.4% vs. 90.8%, $p = 0.298$ (Fig. 2A). However, a statistically significant difference in DFS was observed between the two groups, with the IDC + DCIS group having a better 5-year DFS of 90.6% than the 83.5% in the IDC group, $p = 0.041$ (Fig. 2B).

Univariate and multivariate analyses of the prognostic factors influencing OS and DFS are presented in Table 2.

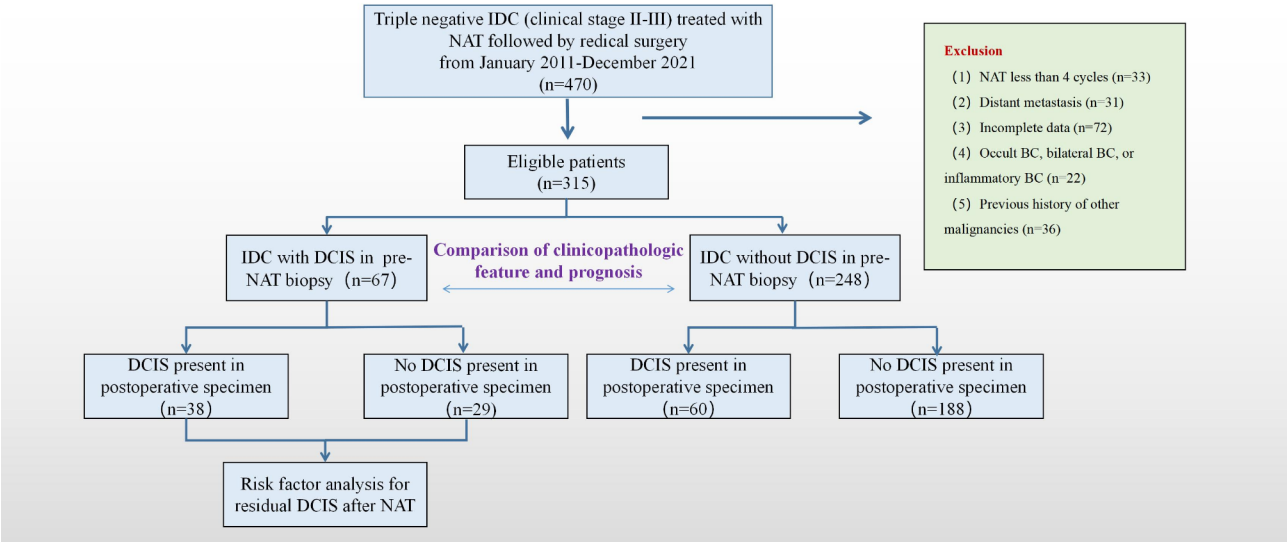

Fig. 1 Study flow chart

Table 1 Clinicopathologic features of the patients in the IDC + DCIS group and IDC group

Variables	IDC (*n* = 248) (*n* %)	IDC + DCIS (*n* = 67) (*n* %)	*P* value
Age at diagnosis (year)			0.198
≤40	59 (23.8)	11 (16.4)	
>40	189 (76.2)	56 (83.6)	
Family history of breast cancer			0.105
Presence	6 (2.4)	5 (7.5)	
Absence	242 (97.6)	62 (92.5)	
Neoadjuvant immunotherapy			0.462
Presence	19 (7.7)	7 (10.4)	
Absence	229 (92.3)	60 (89.6)	
Tumor location			0.727
Central portion	10 (4.0)	4 (6.0)	
Non-central portion	238 (96.0)	63 (94.0)	
Clinical T stage			0.473
T1-T2	218 (87.9)	61 (91.0)	
T3-T4	30 (12.1)	6 (9.0)	
Clinical nodal status			0.309
N0	127 (51.2)	39 (58.2)	
N1-N3	121 (48.8)	28 (41.8)	
IDC grade			0.004
Grade 1–2	54 (21.8)	26 (38.8)	
Grade 3	194 (78.2)	41 (61.2)	
IDC Ki-67			< 0.001
≤20%	4 (1.6)	9 (13.4)	
>20%	244 (98.4)	58 (86.6)	
Types of surgery			0.118
Breast-conserving surgery	80 (32.3)	15 (22.4)	
Mastectomy	168 (67.7)	52 (77.6)	
pCR			0.227
Yes	66 (26.6)	13 (19.4)	
No	182 (73.4)	54 (80.6)	
Residual DCIS			< 0.001
Yes	60 (24.2)	38 (56.7)	
No	188 (75.8)	29 (43.3)	
Adjuvant radiotherapy			0.256
Presence	123 (49.6)	28 (41.8)	
Absence	125 (50.4)	39 (58.2)	

Abbreviation: IDC, invasive ductal carcinoma; DCIS, ductal carcinoma in situ; pCR, pathological complete response

Univariate analysis identified several risk factors associated with OS, including the clinical T stage ($p = 0.031$) and clinical node status ($p = 0.016$). In addition, clinical T stage ($p < 0.001$), clinical node status ($p = 0.010$), DCIS on pre-NAT biopsy ($p = 0.042$), IDC grade ($p = 0.093$), and adjuvant radiotherapy ($p = 0.069$) were associated with DFS. The above-related factors and DCIS in pre-NAT biopsy were included in multivariate analysis, and the results revealed that the clinical T3–T4 stage (HR: 3.410; 95% CI, 1.063–10.941; $p = 0.039$) and clinical N1–N3 (HR: 5.920; 95% CI, 1.312–26.710; $p = 0.021$) were independent prognostic factors significantly affecting OS, and clinical T3 stage (HR: 5.490; 95% CI, 2.389–12.615; $p < 0.001$), clinical N1–N3 (HR: 2.959; 95% CI, 1.172–7.469; $p = 0.022$), and IDC with DCIS (HR: 0.502; 95% CI, 0.284–0.952; $p = 0.048$) were independent prognostic factors for DFS.

Risk factors associated with residual DCIS after NAT

The predictive factors for residual DCIS after NAT in patients with IDC and DCIS components are listed in Table 3. Univariate analysis demonstrated that the clinical T stage ($p = 0.025$) and clinical node status ($p = 0.008$) correlated with residual DCIS after NAT. Multivariate analysis indicated that clinical T3–T4 stage (OR = 3.891; 95% CI, 1.320–15.219, $p = 0.040$) and clinical N1–N3

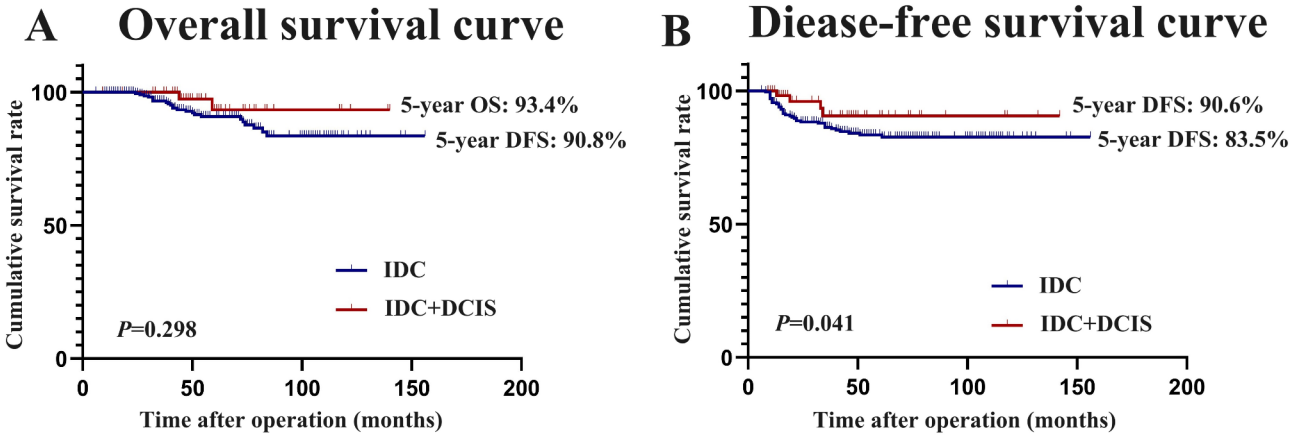

Fig. 2 Survival curves of patients with triple-negative invasive ductal carcinoma with and without a ductal carcinoma in situ component. A overall survival; B disease-free survival

(OR = 4.500; 95% CI, 1.495–13.564, $p = 0.012$) were independent preoperative predictors of residual DCIS after NAT.

Discussion

In the pathogenesis of breast cancer, the prevailing theory is that both DCIS and IDC originate from a common cell lineage, proliferating from a single normal cell ([14]. DCIS is considered a non-specific precursor of IDC, and approximately 30% of DCIS cases may progress to become IDC ([15]. Studies have explored the mechanism of DCIS evolution into IDC at the immune cell infiltration ([16], tumor microenvironment ([17, 18], and epigenetic levels ([19]. Therefore, certain patients with IDC may have a DCIS component, and compared with pure IDC, the presence of DCIS in IDC affects the choice of surgical method and prognosis ([20–22]. However, the proportion of patients with triple-negative IDC and DCIS components is relatively low, and few relevant studies have been reported, especially on those who have received NAT. This study explored the differences in clinicopathological characteristics and prognosis between the IDC and IDC + DCIS groups and the risk factors for residual DCIS after NAT in patients with IDC + DCIS.

A previous study demonstrated that in IDC + DCIS, the proportion of triple-negative molecular types was relatively low, whereas the proportions of HER2-positive and HR-positive types were high (approximately 37.3–43.7%) ([22, 23]. Among the patients with triple-negative IDC included in the current study, the proportion of patients with DCIS was 21.2% (67/315), which was lower than that of patients with breast cancer and other molecular types, consistent with previous reports ([22–24]. In addition, studies have shown that compared to patients with pure IDC, patients with IDC and DCIS have specific clinicopathological characteristics, such as older age, a higher proportion of relevant family history, less lymphovascular invasion, and lower histologic grade ([25, 26]. Similar to the previous studies, the current study found that among patients with TNBC, the proportion of histological grade G3 (78.2% vs. 61.2%, $p = 0.004$) and Ki-67 > 20% (98.4% vs. 86.6%, $p < 0.001$) in patients with IDC and DCIS was significantly lower than in patients with IDC without DCIS. In addition, patients with IDC and DCIS were more likely to be older and have a relevant family history; however, the difference was not statistically significant ($p > 0.05$). These results suggest that among patients with triple-negative IDC, those with a DCIS component exhibit less biological aggressiveness ([27].

However, the effect of DCIS on the prognosis of patients with IDC remains controversial. Lee et al. analyzed 818 breast cancer patients including 224 patients with isolated IDC and 594 patients with IDC + DCIS, and found that in patients with IDC, the presence of DCIS did not affect the 5-year OS after adjustment for confounders (HR: 0.86; 95% CI, 0.48–1.54; $p = 0.608$) ([21]. Conversely, a retrospective study of 358 patients with TNBC demonstrated less invasive biological characteristics and better 5-year DFS (87.9% vs. 82.6%, $p = 0.045$) in patients with IDC and DCIS than in patients with IDC without DCIS ([28]. The reasons for the above different results may be related to the different clinicopathological characteristics of the included patients, such as TNM stage, NAT regimens, and molecular type. This study focused on patients with stage II–III triple-negative IDC undergoing NAT, and the results showed that in this specific population, the DFS in patients with IDC and DCIS was significantly better than that in patients without DCIS (90.6% vs. 83.5%, $p = 0.041$), and after eliminating confounding factors, the presence DCIS was still a protective factor for DFS in patients with triple-negative IDC (HR: 0.502; 95% CI, 0.284–0.952; $p = 0.048$). Therefore, we believe that patients with triple-negative IDC and DCIS

Table 2 The univariate and multivariate analyses of prognostic factors influencing OS and DFS

Variables	Overall survival				Disease-free survival			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
	HR (95%CI)	*P*	HR (95%CI)	*P*	HR (95%CI)	*P*	HR (95%CI)	*P*
Age at diagnosis (years)								
≤40	Reference				Reference			
>40	0.989 (0.274–3.568)	0.986			0.788 (0.329–1.888)	0.593		
Family history of breast cancer								
Absence	Reference				Reference			
Presence	0.673 (0.207–12.901)	0.489			0.542 (0.211–14.921)	0.283		
Neoadjuvant immunotherapy								
Absence	Reference				Reference			
Presence	0.791 (0.291–2.801)	0.339			0.713 (0.352–1.942)	0.150		
Tumor location								
Central portion	Reference				Reference			
Non-central portion	0.579 (0.306–12.401)	0.370			0.428 (0.281–10.911)	0.175		
Clinical T stage								
T1-T2	Reference				Reference		Reference	
T3-T4	3.583 (1.123–11.432)	0.031	3.410 (1.063–10.941)	0.039	5.654 (2.484–12.873)	< 0.001	5.490 (2.389–12.615)	< 0.001
Clinical nodal status								
N0	Reference				Reference			
N1-N3	6.296 (1.406–28.187)	0.016	5.920 (1.312–26.710)	0.021	3.346 (1.336–8.381)	0.010	2.959 (1.172–7.469)	0.022
DCIS in pre-NAT biopsy								
IDC without DCIS	Reference				Reference			
IDC with DCIS	0.695 (0.366–1.318)	0.265	0.703 (0.206–2.190)	0.342	0.479 (0.217–0.863)	0.042	0.502 (0.284–0.952)	0.048
IDC grade								
Grade 1–2	Reference				Reference		Reference	
Grade 3	2.158 (0.493–7.858)	0.260			2.911 (0.887–7.986)	0.093	1.826 (0.676–4.935)	0.235
IDC Ki-67								
≤20%	Reference				Reference			
>20%	2.950 (0.552–18.081)	0.487			3.522 (0.611–11.351)	0.235		
Types of surgery								
Breast-conserving surgery	Reference				Reference			
Mastectomy	0.625 (0.216–1.804)	0.384			0.830 (0.367–1.879)	0.655		
pCR								
No	Reference				Reference		Reference	
Yes	0.412 (0.238–4.603)	0.158			0.373 (0.204–0.783)	0.030	0.402 (0.221–0.872)	0.035
Residual DCIS								
No	Reference				Reference			
Yes	1.110 (0.347–3.547)	0.860			1.228 (0.530–2.847)	0.632		
Adjuvant radiotherapy								
Absence	Reference				Reference		Reference	
Presence	3.941 (0.801–15.294)	0.144			2.542 (0.911–8.210)	0.069	1.590 (0.619–5.218)	0.585

Abbreviation: IDC, invasive ductal carcinoma; DCIS, ductal carcinoma in situ; pCR, pathological complete response; OS, overall survival; DFS, disease-free survival

components are characterized by weak invasiveness and low recurrence risk. Although the incidence of residual DCIS after NAT is high, they often have a favorable prognosis if appropriate surgical methods are selected.

This study found that the incidence of residual DCIS in patients with IDC and DCIS after NAT was significantly higher than that in patients without DCIS (56.7% vs. 24.2%, $p < 0.001$); extensive DCIS could affect the implementation of BCS; and the sensitivity and specificity of

Table 3 Predictive factors for residual DCIS after NAT in patients with IDC and DCIS components

Variables	Residual DCIS	Univariate analysis		Multivariate analysis	
		OR (95%CI)	*P*	OR (95%CI)	*P*
Age at diagnosis (year)					
<50	7/11 (63.6)	Reference			
≥50	31/56 (55.4)	0.709 (0.186–2.697)	0.613		
Family history of breast cancer					
Presence	3/5 (60.0)	Reference			
Absence	35/62 (56.5)	0.824 (0.307–4.128)	0.790		
Tumor location					
Central portion	2/4 (50.0)	Reference			
Non-central portion	36/63 (57.1)	1.620 (0.781–5.211)	0.498		
Clinical T stage					
T1-T2	33/62 (53.2)	Reference			
T3-T4	6/6 (100.0)	3.421 (1.120-13.421)	0.025	3.891 (1.320-15.219)	0.040
Clinical nodal status					
N0	11/29 (37.9)	Reference			
N1-N3	27/38 (62.1)	4.017 (1.439–11.214)	0.008	4.500 (1.495–13.564)	0.012
IDC grade					
Grade 1–2	17/26 (65.4)	Reference			
Grade 3	21/41 (51.2)	0.556 (0.202–1.532)	0.256		
IDC Ki-67					
≤20%	8/9 (88.9)	Reference			
>20%	30/58 (11.1)	0.512 (0.299–0.910)	0.037	0.560 (0.341–0.951)	0.046

Abbreviation: IDC, invasive ductal carcinoma; DCIS, ductal carcinoma in situ; NAT, neoadjuvant therapy

radiological prediction of residual DCIS are still not ideal ([29]. Therefore, it is necessary to predict the risk factors for residual DCIS after NAT in patients with IDC and DCIS to determine the indications for BCS after NAT. Ploumen et al. found that in HER2-positive patients with IDC and DCIS, the ER status ($p < 0.001$), clinical T stage ($p = 0.006$), and years since diagnosis ($p = 0.003$) were associated with DCIS response after NAT ([20]. A study of 280 HER2-positive patients with clinical T1-2,N0-1 showed that the clinical node status and HR status were associated with the prediction of residual disease in the breast or nodes after NAT ([30]. Similar to the above report, the results of this study also showed that clinical T3–T4 (OR = 3.891; 95% CI, 1.320–15.219, $p = 0.040$) and N1–N3 were risk factors for residual DCIS after NAT in patients with triple-negative IDC with DCIS (OR = 4.500; 95% CI, 1.495–13.564, $p = 0.012$). The results of this study can be used to assess the risk of residual DCIS after NAT in patients with triple-negative IDC and DCIS, and facilitate the formulation of surgical plans.

This study had several limitations. First, as a retrospective analysis, it may be subject to potential selection bias. Second, the proportion of patients with triple-negative IDC who received NAT was relatively low, and the small sample size limited the robustness of the statistical analysis. Finally, while neoadjuvant immunotherapy has shown promising results in specific TNBC populations, its adoption was limited for the year chosen for this study, making it challenging to accurately measure its effects in patients with triple-negative IDC and DCIS. Further large-sample, randomized controlled trials are needed to better characterize treatment outcomes in these patients.

Overall, our study demonstrates that patients with triple-negative IDC and a DCIS component have less tumor aggressiveness than those without DCIS, and better survival outcomes can be observed after NAT. Additionally, clinical T and N stages are risk factors for residual DCIS after NAT in patients with triple-negative IDC and a DCIS component.

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Author contributions
Contributions: (I) conception and design: SCZ, WX; (II) administrative support: SCZ (III) provision of study materials or patients: SCZ, ZHH and YT; (IV) collection and assembly of data: SCZ and LL; (V) data analysis and interpretation: LL, ZHH and YT. All authors read and approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
All enrolled patients sign written informed consent to participate in the study. The study was conducted per STARD reporting guidelines. All the procedures followed the ethical standards of the World Medical Association Declaration

of Helsinki. The Institutional Review Board Committee of the institutions approved this study.

Consent for publication
Not Applicable.

Competing interests
The authors declare no competing interests.

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References

1. Denkert C, Liedtke C, Tutt A, et al. Molecular alterations in triple-negative breast cancer-the road to new treatment strategies. Lancet. 2017;89(10087):2430–42.
2. Mahtani R, Kittaneh M, Kalinsky K, et al. Advances in therapeutic approaches for Triple-Negative breast cancer. Clin Breast Cancer. 2021;21(5):383–90.
3. Garrido-Castro AC, Lin NU, Polyak K. Insights into molecular classifications of Triple-Negative breast cancer: improving patient selection for treatment. Cancer Discov. 2019;9(2):176–98.
4. Galindo García C, Díaz Acedo R, Artacho Criado S et al. Effectiveness and safety of neoadjuvant therapy in triple-negative breast cancer in a real-world population. Farm Hosp. 2024;S1130-6343(24)00050– 3.
5. Rogers C, Cobb AN, Lloren JIC, et al. National trends in neoadjuvant chemotherapy utilization in patients with early-stage node-negative triple-negative breast cancer: the impact of the CREATE-X trial. Breast Cancer Res Treat. 2024;203(2):317–28.
6. Johnson KC, Koestler DC, Fleischer T, et al. DNA methylation in ductal carcinoma in situ related with future development of invasive breast cancer. Clin Epigenetics. 2015;7(1):75.
7. Cain H, Macpherson IR, Beresford M, et al. Neoadjuvant therapy in early breast cancer: treatment considerations and common debates in practice. Clin Oncol (R Coll Radiol). 2017;9(10):642–52.
8. Goldberg H, Zandbank J, Kent V, et al. Chemotherapy May eradicate ductal carcinoma in situ (DCIS) but not the associated microcalcifications. Eur J Surg Oncol. 2017;43(8):1415–20.
9. Kole AJ, Park HS, Johnson SB, et al. Overall survival is improved when DCIS accompanies invasive breast cancer. Sci Rep. 2019;9(1):9934.
10. Pang JM, Gorringe KL, Fox SB. Ductal carcinoma in situ-update on risk assessment and management. Histopathology. 2016;68(1):96–109.
11. Dzierzanowski M, Melville KA, Barnes PJ, et al. Ductal carcinoma in situ in core biopsies containing invasive breast cancer: correlation with extensive intraductal component and lumpectomy margins. J Surg Oncol. 2005;90(2):71–6.
12. Hu J, Fung MW, et al. Improved prognostication for the updated AJCC breast cancer pathological prognostic staging varied in Higher-Stage groups. Clin Breast Cancer. 2020;20(3):253–e2617.
13. Jiang Z, Li J, Chen J, et al. Chinese society of clinical oncology (CSCO) breast cancer guidelines 2022. Transl Breast Cancer Res. 2022;3:13.
14. Casasent AK, Schalck A, Gao R, et al. Multiclonal invasion in breast tumors identified by topographic single cell sequencing. Cell. 2018;172(1–2):205–e21712.
15. Lagios MD, Silverstein MJ. Ductal carcinoma in situ: recent history and areas of controversy. Breast J. 2015;21(1):21–6.
16. Niwińska A, Olszewski WP. The role of stromal immune microenvironment in the progression of ductal carcinoma in situ (DCIS) to invasive breast cancer. Breast Cancer Res. 2021;24(1):118.
17. Dawoud MM, Jones DT, Chelala C, Abdou AG, Dreger SA, Asaad N, Abd El-Wahed M, Jones L. Expression profile of myoepithelial cells in DCIS: do they change from protective angels to wicked witches?? Appl Immunohistochem Mol Morphol. 2022;30(6):397–409.
18. Rebbeck CA, Xian J, Bornelöv S, et al. Gene expression signatures of individual ductal carcinoma in situ lesions identify processes and biomarkers associated with progression towards invasive ductal carcinoma. Nat Commun. 2022;13(1):3399.
19. DeVaux RS, Herschkowitz JI. Beyond DNA: the role of epigenetics in the premalignant progression of breast cancer. J Mammary Gland Biol Neoplasia. 2018;23(4):223–35.
20. Ploumen RAW, Claassens EL, Kooreman LFS, et al. Pathologic complete response of ductal carcinoma in situ to neoadjuvant systemic therapy in HER2-positive invasive breast cancer patients: a nationwide analysis. Breast Cancer Res Treat. 2023;201(2):227–35.
21. Lee WP, Shetty SS, Seah CMJ, et al. Does concomitant ductal carcinoma in situ affect the clinical outcome in breast cancer patients with invasive ductal carcinoma: an Asian perspective. Cancer Rep (Hoboken). 2022;5(9):e1646.
22. Groen EJ, van der Noordaa MEM, Schaapveld M, et al. Pathologic response of ductal carcinoma in situ to neoadjuvant systemic treatment in HER2-positive breast cancer. Breast Cancer Res Treat. 2021;189(1):213–24.
23. von Minckwitz G, Darb-Esfahani S, Loibl S, et al. Responsiveness of adjacent ductal carcinoma in situ and changes in HER2 status after neoadjuvant chemotherapy/trastuzumab treatment in early breast cancer–results from the GeparQuattro study (GBG 40). Breast Cancer Res Treat. 2012;132(3):863–70.
24. Takahashi S, Thike AA, Koh VCY, et al. Triple-negative and HER2 positive ductal carcinoma in situ of the breast: characteristics, behavior, and biomarker profile. Virchows Arch. 2018;473(3):275–83.
25. Guan X, Xu G, Shi A, et al. Comparison of clinicopathological characteristics and prognosis among patients with pure invasive ductal carcinoma, invasive ductal carcinoma coexisted with invasive micropapillary carcinoma, and invasive ductal carcinoma coexisted with ductal carcinoma in situ: A retrospective cohort study. Med (Baltim). 2020;99(50):e23487.
26. Goh CW, Wu J, Ding S, et al. Invasive ductal carcinoma with coexisting ductal carcinoma in situ (IDC/DCIS) versus pure invasive ductal carcinoma (IDC): a comparison of clinicopathological characteristics, molecular subtypes, and clinical outcomes. J Cancer Res Clin Oncol. 2019;145(7):1877–86.
27. Thike AA, Iqbal J, Cheok PY, et al. Ductal carcinoma in situ associated with triple negative invasive breast cancer: evidence for a precursor-product relationship. J Clin Pathol. 2013;66(8):665–70.
28. Liu Y, Yu T. Clinicopathological characteristics and prognosis of triple-negative breast cancer invasive ductal carcinoma with ductal carcinoma in situ. J Cancer Res Clin Oncol. 2023;149(13):11181–91.
29. Ploumen RAW, de Mooij CM, Gommers S, et al. Imaging findings for response evaluation of ductal carcinoma in situ in breast cancer patients treated with neoadjuvant systemic therapy: a systematic review and meta-analysis. Eur Radiol. 2023;33(8):5423–35.
30. Sun S, van la Parra RFD, Rauch GM, et al. Patient selection for clinical trials eliminating surgery for HER2-Positive breast cancer treated with neoadjuvant systemic therapy. Ann Surg Oncol. 2019;26(10):3071–9.

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