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Prognostic implications of ductal carcinoma *in situ* components in *BRCA1/2*-positive breast cancer: a retrospective cohort study

Kyung-Hwak Yoon, Eun-Kyu Kim, Hee-Chul Shin

Department of Surgery, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Korea

Purpose: Although the breast cancer susceptibility gene *(BRCA)*-associated invasive breast cancer is well studied, there are limited reports on ductal carcinoma *in situ* (DCIS) in patients with *BRCA1/2* mutations. This study aims to evaluate the differential prognostic effect of DCIS in breast cancer patients with pathologic variants of *BRCA1/2* genes.
Methods: Breast cancer patients who tested positive for *BRCA1/2* mutations between August 2003 and January 2022 at a single tertiary referral center were retrospectively analyzed. Survival outcomes were compared between patients with both invasive ductal carcinoma (IDC) and DCIS (IDC-DCIS group, n = 121) and those with IDC alone (IDC group, n = 36).
Results: Of the 157 patients, 65 (41.4%) exhibited mutations in *BRCA1*, 90 (57.3%) in *BRCA2*, and 2 (1.3%) in both *BRCA1/2*. DCIS components were more frequently found in *BRCA2* pathological variants (*BRCA1*, 46 [38.0%] *vs*. *BRCA2*, 76 [62.4%]; P = 0.030). No statistically significant difference was found in 10-year recurrence-free survival (IDC-DCIS, 89.3% *vs*. IDC, 83.6%; P = 0.989). Subgroup analysis indicated that the DCIS component correlated with improved survival outcomes in the *BRCA1* subgroup (*BRCA1* IDC-DCIS, 85.5% *vs*. *BRCA1* IDC, 51.0%; P = 0.024). Conversely, in the *BRCA2* subgroup, IDC-DCIS patients exhibited a worse prognosis (*BRCA1* IDC-DCIS, 85.5% *vs*. *BRCA2* IDC-DCIS, 65.8%; P = 0.045).
Conclusion: The presence of a DCIS component carries varied prognostic significance in *BRCA1* and *BRCA2* mutations. A tailored approach may be necessary when determining treatment options for breast cancer patients with *BRCA1/2* mutations based on the presence of DCIS.
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Key Words: Breast neoplasms, BRCA1 protein, BRCA2 protein, Breast carcinoma *in situ*

INTRODUCTION

As breast cancer is the most prevalent malignancy in women globally, several risk factors have been identified. Genetic factors are crucial in breast cancer, as roughly 5%–10% of all tumors are associated with inheritable genetic mutations [1,2]. The most frequent genetic mutations tied to hereditary breast cancer are the breast cancer susceptibility genes (*BRCA1* and *BRCA2*) [3,4]. Women possessing *BRCA1/2* mutations have a reported 40 to 70% cumulative risk of developing breast cancer throughout their lifetime [5,6].

Genetic counseling and *BRCA* testing for patients and families at high risk have seen an uptick in clinical settings [7]. For individuals who test positive for *BRCA* mutations, annual screening using breast MRI and mammography is recommended at an early age. Risk-reducing prophylactic mastectomy is also presented as an option [8]. Consequently, the likelihood of incidental detection of early breast cancer and precancerous lesions in these patients is on the rise [9].

A plethora of studies have concentrated on survival outcomes

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Corresponding Author: Hee-Chul Shin
Department of Surgery, Seoul National University Bundang Hospital, 82 Gumi-ro 173 Beon-gil, Bundang-gu, Seongnam 13620, Korea
Tel: +82-31-787-7097, **Fax:** +82-31-787-4078
E-mail: dradam77@naver.com
ORCID: https://orcid.org/0000-0001-6512-2218

and pertinent prognostic factors for patients with *BRCA1*- or *BRCA2*-associated invasive ductal carcinoma (IDC). Ductal carcinoma *in situ* (DCIS), which is considered a precursor of IDC, is often found together with IDC on pathology. Claus et al. [10] reported *BRCA1/2* prevalence rates in DCIS to be similar to those in IDC based on population studies. Nonetheless, research is scant regarding the prognostic implications of DCIS in breast cancer patients harboring *BRCA1/2* mutations.

In earlier studies not centered on *BRCA1/2*-related breast cancer, the presence of DCIS in invasive carcinoma correlated with enhanced disease-free survival (DFS) and was deemed a positive prognostic indicator [11,12]. Given that invasive tumors might originate from antecedent DCIS, malignancies with concurrent DCIS likely manifest a delay in transformation, exhibiting a more indolent course [13]. IDC-DCIS has been associated with beneficial clinical traits, such as smaller tumor dimensions, lower grade, and reduced lymph node involvement [14]. Contrarily, some investigations have unveiled findings wherein IDC-DCIS displays heightened biological aggression [15].

In this study, our objective was to ascertain whether concomitant carcinoma *in situ* influences long-term recurrence-free survival outcomes in *BRCA1/2*-associated breast cancer patients. A subgroup assessment was conducted for both *BRCA1* and *BRCA2* mutation carriers. Additionally, multivariable analyses were executed to pinpoint potential predictive elements for recurrence in *BRCA*-related breast cancer.

METHODS

Study population

We retrospectively analyzed patients who underwent curative resection for breast cancer with a final pathological diagnosis of IDC between August 2003 and January 2022 at Seoul National University Bundang Hospital. Among them, 201 patients who tested positive for *BRCA1/2* mutations via genetic testing were included. Patients diagnosed solely with DCIS, those with bilateral breast cancer, stage IV cancer patients, and those lacking comprehensive histologic data were excluded. Ultimately, 157 patients were considered for analysis. Based on the presence of DCIS components on pathologic evaluation, patients were categorized into 2 groups: 121 patients had both invasive cancer and DCIS (IDC-DCIS group), while 36 patients exhibited IDC only (IDC group).

The study received approval from the Institutional Review Board (IRB) of Seoul National University Bundang Hospital (No. B-2309-852-101) and was conducted following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting observational studies [16]. Informed consent from the study participants was waived by the IRB due to the retrospective nature of the study. The trial was registered on the Clinical Research Information Service (KCT0009513, Date of registration: 05/06/2024, http://www.cris.nih.go.kr), which is approved by the WHO International Clinical Trials Registry Platform.

Data collection and definitions

Demographic data for study participants were sourced from a review of medical records. Information pertaining to age at diagnosis, tumor size, nodal status, histologic grade of the tumor, estrogen receptor (ER) status, progesterone receptor (PR) status, human epidermal growth factor receptor-2 (HER-2) expression, surgical procedures, chemotherapy, radiotherapy, bilateral oophorectomy, family history of breast cancer, and details on recurrence were extracted from these records. "Recurrence" encompassed both locoregional and distant recurrence. Contralateral breast cancer was omitted due to the challenges in differentiating genuine recurrence from a new primary malignancy. Follow-up details were recorded up to the most recent hospital visit for each patient. The 10-year DFS was calculated, with events censored at 10 years.

Statistical analysis

All statistical evaluations were conducted using IBM SPSS Statistics ver. 28.0 (IBM Corp). Continuous variables were compared using the Student t-test, while categorical variables were assessed using the chi-square test or Fisher exact test. Survival analysis was performed using the Kaplan-Meier method and the log-rank test. Both univariate and multivariate regression analyses utilized Cox proportional hazard models. All P-values were 2-sided, and $P < 0.05$ was considered statistically significant.

RESULTS

A total of 157 cases were evaluated in this study. The participants included carriers of *BRCA1* mutations (n = 65, 41.4%), *BRCA2* mutations (n = 90, 57.3%), or both (n = 2, 1.3%). The baseline clinical characteristics of the IDC-DCIS group and IDC group are detailed in Table 1. No statistically significant difference was observed regarding age at diagnosis between the groups. However, distinct expression patterns of *BRCA1/2* mutations emerged. The IDC-DCIS group exhibited more *BRCA2* mutations (IDC-DCIS, 76 [62.4%] *vs.* IDC, 16 [44.4%]; P = 0.050), whereas the IDC group had a higher mutation rate of *BRCA1* (IDC-DCIS, 46 [38.0%] *vs.* IDC, 21 [58.3%]; P = 0.030). In terms of adjuvant treatment, the IDC group was more frequently administered both hormone therapy (IDC-DCIS, 43 [35.5%] *vs.* IDC, 30 [83.3%]; P < 0.001) and chemotherapy (IDC-DCIS, 100 [82.6%] *vs.* IDC, 35 [97.2%]; P = 0.027).

Pathological features between the groups were also compared. There was no significant distinction in tumor size or stage. However, the IDC-DCIS group demonstrated increased

Table 1. Clinicopathologic characteristics of patients with IDC-DCIS *vs*. IDC alone

Characteristic	Total	IDC-DCIS group	IDC group	P-value
No. of patients	157	121	36	
Age (yr)	43 (23–72)	42 (23–72)	44 (29–72)	0.653
Sex				>0.999
Male	3 (1.9)	3 (2.5)	0 (0)	
Female	154 (98.1)	118 (97.5)	36 (100)	
BRCA pathological variant				
BRCA1	67 (42.7)	46 (38.0)	21 (58.3)	0.030
BRCA2	92 (58.6)	76 (62.4)	16 (44.4)	0.050
Family history				
Breast cancer	100 (63.7)	76 (62.8)	24 (66.7)	0.673
Ovarian cancer	20 (12.7)	18 (14.9)	2 (5.6)	0.167
First-degree relative with breast cancer				0.372
0	86 (54.8)	69 (57.0)	17 (47.2)	
1	54 (34.4)	38 (31.4)	16 (44.4)	
2+	17 (10.8)	14 (11.6)	3 (8.3)	
Operation method				0.252
Breast-conserving surgery	85 (54.2)	62 (51.2)	23 (63.9)	
Total mastectomy	72 (45.8)	59 (48.8)	13 (36.1)	
Hormone therapy	84 (53.5)	78 (64.5)	6 (16.7)	<0.001
Chemotherapy	135 (86.0)	100 (82.6)	35 (97.2)	0.027
Radiation therapy	39 (24.8)	32 (26.4)	7 (19.4)	0.393
Salpingo-oophorectomy	100 (63.7)	78 (64.5)	22 (61.1)	0.714
Recurrence	29 (18.5)	22 (18.2)	7 (19.4)	0.874
Ipsilateral breast	9 (5.7)	7 (5.8)	2 (5.6)	>0.999
Locoregional	7 (4.5)	5 (4.1)	2 (5.6)	0.660
Distant	20 (12.7)	17 (14.0)	3 (8.3)	0.569
Tumor size (cm)	2.5 (0.1–9.5)	2.4 (0.1–9.5)	2.6 (1–8)	0.169
Tumor stage				0.099
T1	69 (43.9)	58 (47.9)	11 (30.6)	
T2	72 (45.9)	49 (40.5)	23 (63.9)	
T3	12 (7.6)	10 (8.3)	2 (5.6)	
T4	4 (2.5)	4 (3.3)	0 (0)	
Nodal status				0.259
N0	74 (47.1)	60 (49.6)	14 (38.9)	
N+	83 (52.9)	61 (50.4)	22 (61.1)	
Combined ER status and HER2				<0.001
ER+/HER2–	74 (47.1)	69 (57)	5 (13.9)	
ER+/HER2+	5 (3.2)	5 (4.1)	0 (0)	
ER–/HER2+	45 (28.7)	44 (36.4)	1 (2.8)	
ER–/HER2–	33 (21)	3 (2.5)	30 (83.3)	
Ki-67 (%)				0.065
<14	24 (15.3)	22 (18.2)	2 (5.6)	
≥14	125 (79.6)	93 (76.9)	32 (88.9)	
Unknown	8 (5.1)	6 (5.0)	2 (5.6)	
Histologic grade				0.004
I	4 (2.5)	4 (3.3)	0 (0)	
II	59 (37.6)	53 (43.8)	6 (16.7)	
III	94 (59.9)	64 (52.9)	30 (83.3)	

Values are presented as number only, mean (range), or number (%).
IDC, invasive ductal carcinoma; DCIS, ductal carcinoma *in situ*; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2.

expression of hormone receptors (IDC-DCIS, 69 [57.0%] *vs*. IDC, 5 [13.9%]; P < 0.001). Conversely, the IDC group displayed a higher histologic grade (P = 0.004).

For the entire study population, the 3-, 5-, and 10-year DFS rates were 92.0%, 87.8%, and 72.1%, respectively. Recurrence rates appeared comparable between the IDC and IDC-DCIS

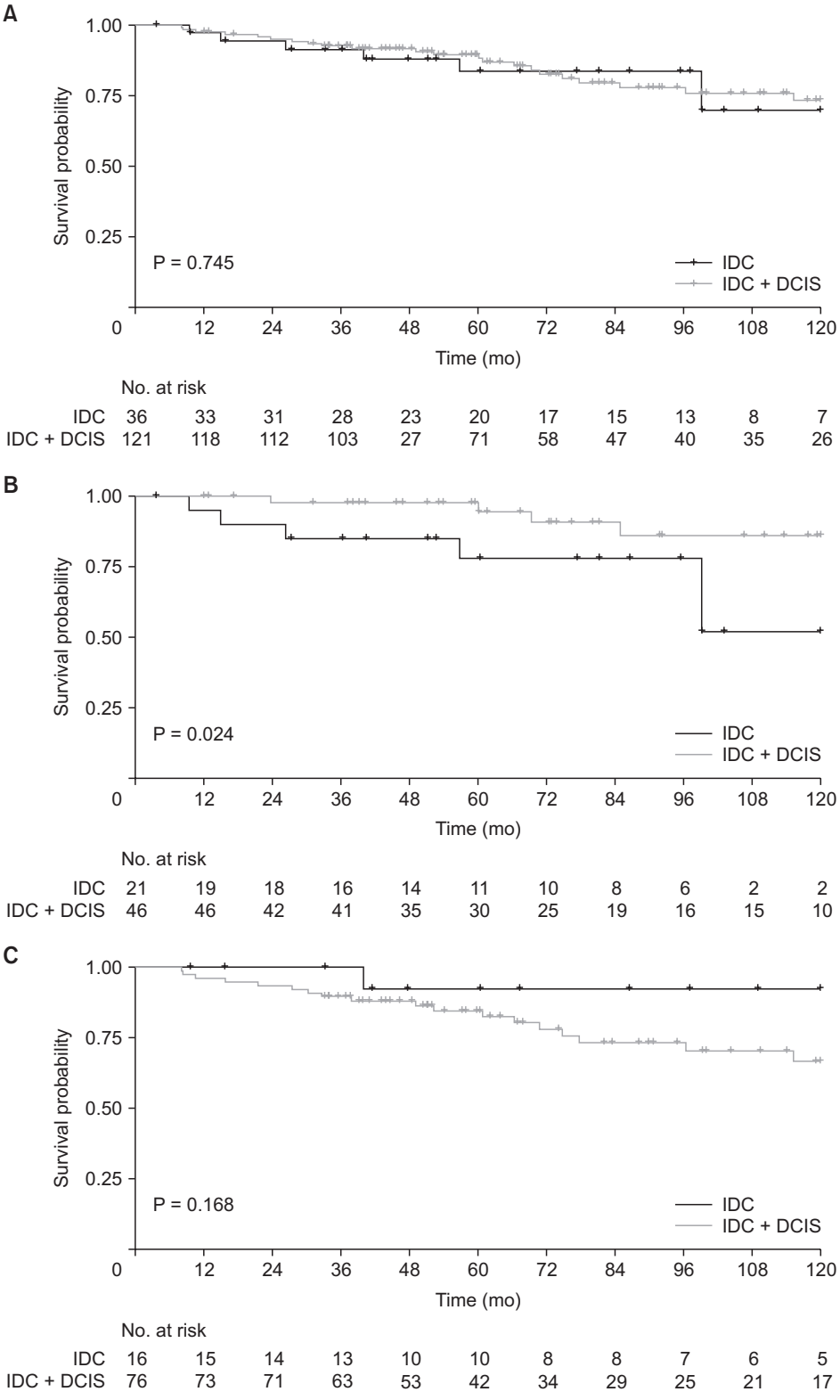


Fig. 1. Disease-free survival according to the presence of ductal carcinoma *in situ* component. (A) All patients. (B) *BRCA1* subgroup. (C) *BRCA2* subgroup. IDC, invasive ductal carcinoma; DCIS, ductal carcinoma *in situ*.

groups (IDC-DCIS, 43 [35.5%] *vs.* IDC, 12 [33.37%]; P = 0.808). The 10-year DFS difference between the 2 groups was not statistically significant (IDC-DCIS, 72.9% *vs.* IDC, 69.2%; P = 0.745) (Fig. 1A).

Subgroup analyses were conducted separately for *BRCA1* and *BRCA2* mutation carriers (Table 2). Within the *BRCA1* subgroup, IDC-DCIS was linked to higher rates of hormone receptor expression (IDC-DCIS, 8 [17.4%] *vs.* IDC, 0; P = 0.016). Notably,

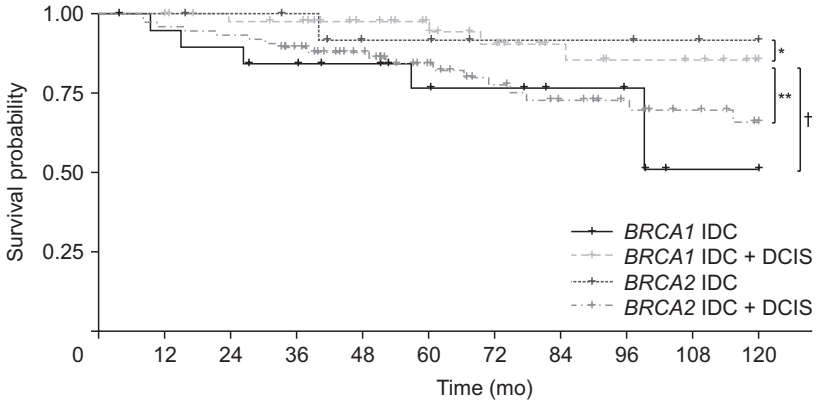
Table 2. Subgroup analysis of patients with *BRCA1* and *BRCA2* mutations

Variable	*BRCA1*			*BRCA2*		
	IDC-DCIS group (n = 46)	IDC group (n = 21)	P-value	IDC-DCIS group (n = 76)	IDC group (n = 16)	P-value
Age (yr)	38 (32–45)	37 (33–50)	0.660	39 (35–55)	46 (36–55)	0.418
Sex			>0.999			>0.999
Male	0 (0)	0 (0)		3 (3.9)	0 (0)	
Female	46 (100)	21 (100)		73 (96.1)	16 (100)	
Operation method			0.872			0.137
Breast-conserving surgery	31 (67.4)	13 (61.9)		32 (42.1)	10 (62.5)	
Total mastectomy	15 (32.6)	8 (38.1)		44 (57.9)	6 (37.5)	
Tumor size (cm)	2.2 (1.7–3.0)	2.7 (1.9–3.6)	0.140	2.1 (1.1–3.0)	2.2 (1.8–2.3)	0.749
Tumor stage			0.595			0.062
T1	19 (41.3)	6 (28.6)		39 (51.3)	5 (31.3)	
T2	24 (52.2)	13 (61.9)		26 (34.2)	11 (68.8)	
T3	3 (6.5)	2 (9.5)		7 (9.2)	0 (0)	
T4	0 (0)	0 (0)		4 (5.3)	0 (0)	
Nodal status			0.182			>0.999
N0	25 (54.3)	7 (33.3)		36 (48.0)	7 (46.7)	
N+	21 (45.7)	14 (66.7)		40 (52.6)	9 (56.3)	
Combined ER status and HER2			0.016			<0.001
ER+/HER2–	8 (17.4)	0 (0)		61 (80.3)	5 (31.2)	
ER+/HER2+	2 (4.3)	0 (0)		3 (3.9)	0 (0)	
ER–/HER2+	3 (6.5)	1 (4.8)		0 (0)	0 (0)	
ER–/HER2–	33 (71.7)	20 (95.2)		12 (15.8)	11 (68.8)	
Ki-67 (%)			0.787			0.211
<14	2 (4.3)	1 (4.8)		20 (26.3)	1 (6.3)	
≥14	43 (93.5)	19 (90.5)		51 (67.1)	14 (87.5)	
Unknown	1 (2.2)	1 (4.8)		5 (6.6)	1 (6.3)	
Histologic grade			0.185			0.073
I	1 (2.2)	0 (0)		3 (3.9)	0 (0)	
II	9 (19.6)	1 (4.8)		44 (57.9)	5 (1.3)	
III	36 (78.3)	20 (95.2)		29 (38.2)	11 (68.8)	
Hormone therapy	14 (30.4)	0 (0)	0.003	65 (85.5)	6 (40.0)	0.001
Chemotherapy	41 (89.1)	21 (100)	0.173	60 (78.9)	15 (93.8)	0.288
Radiation therapy	39 (84.8)	18 (85.7)	>0.999	51 (67.1)	11 (73.3)	0.899
Salpingo-oophorectomy	34 (73.9)	13 (61.9)	0.479	44 (58.7)	10 (62.5)	0.734
Recurrence	4 (8.7)	6 (28.6)	0.057	18 (24.0)	1 (6.7)	0.285
Ipsilateral breast	3 (6.5)	2 (9.5)	0.645	5 (6.6)	0 (0)	0.583
Locoregional	1 (2.2)	2 (9.5)	0.229	4 (5.3)	0 (0)	>0.999
Distant	1 (2.2)	2 (9.5)	0.229	16 (21.1)	1 (6.3)	0.288

Values are presented as number (range or percentage).
IDC, invasive ductal carcinoma; DCIS, ductal carcinoma *in situ*; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2.

the presence of a DCIS component correlated with a statistically significant improvement in 10-year DFS (IDC-DCIS, 85.5% *vs.* IDC, 51.0%; P = 0.024) (Fig. 1B). In the *BRCA2* subgroup, IDC-DCIS also indicated high rates of hormone receptor expression (IDC-DCIS, 61 [80.3%] *vs.* IDC, 5 [31.2%]; P < 0.001). However, contrary to the *BRCA1* subgroup, IDC-DCIS in the *BRCA2* subgroup was tied to a less favorable prognosis, even though the results were not statistically significant (IDC-DCIS, 65.8% *vs.* IDC, 91.7%; P = 0.114) (Fig. 1C). When compared to *BRCA1* IDC-DCIS, the *BRCA2* IDC+DCIS group showed significantly worse DFS (P = 0.045) (Fig. 2).

Cox regression analysis was utilized to examine risk factors for recurrence (Table 3). In the univariable analysis, younger age at diagnosis was a significant predictor for recurrence (hazard ratio [HR], 2.236; P = 0.049). Patients who underwent salpingo-oophorectomy experienced a substantially reduced risk (HR, 0.106; P < 0.001). Both *BRCA1* IDC (HR, 4.128; P = 0.028) and *BRCA2* IDC-DCIS (HR, 3.234; P = 0.032) presented heightened risks of recurrence in contrast to *BRCA1* IDC-DCIS. In the multivariable analysis, salpingo-oophorectomy was a significant



No. at risk

BRCA1 IDC	20	18	17	15	13	10	9	7	6	2	2
BRCA1 IDC + DCIS	45	45	41	40	34	29	24	18	15	14	9
BRCA2 IDC	15	14	13	12	9	9	7	7	7	6	5
BRCA2 IDC + DCIS	75	72	70	62	52	41	33	28	24	20	16

Fig. 2. Disease-free survival according to *BRCA* mutation type and presence of DCIS component. IDC, invasive ductal carcinoma; DCIS, ductal carcinoma *in situ*. *P = 0.821, **P = 0.045, †P = 0.024.

prognostic factor (HR, 0.112; P < 0.001), and both *BRCA1* IDC (HR, 3.818; P = 0.042) and *BRCA2* IDC-DCIS (HR, 3.582; P = 0.024) persisted as significant risk factors relative to *BRCA1* IDC-DCIS.

DISCUSSION

In the current study, we evaluated whether the presence of a DCIS component influences the prognosis of breast cancer patients with pathologic variants of *BRCA1/2* genes. To our knowledge, this is the first study to focus specifically on the prognostic significance of DCIS in *BRCA1/2*-positive breast cancer. We discovered that patients with DCIS components and those with IDC alone manifested distinct expression patterns for *BRCA1* and *BRCA2* mutations. IDC-DCIS generally exhibited greater expression of hormone receptors and a lower histologic grade. Within *BRCA1* pathological variants, IDC-DCIS correlated with more favorable survival outcomes. Conversely, in *BRCA2*-positive breast cancer, patients with DCIS components displayed higher recurrence rates.

Historical data indicate that *BRCA*-associated DCIS is more frequently detected in patients with *BRCA2* mutations than with *BRCA1* [17,18]. Breast cancer associated with *BRCA1* mutations is characterized by more aggressive attributes, including a triple-negative type and elevated histological grade, and shows transition to invasive carcinoma more rapidly [9,19]. This could elucidate the more abundant occurrence of DCIS in *BRCA2* mutation patients. Our findings harmonize with the prevailing literature, with IDC-DCIS being more affiliated with *BRCA2*.

Although DCIS components are perceived as premalignant lesions in sporadic breast cancer, their role in *BRCA*-associated breast cancer remains under-researched. Traditionally, DCIS was less frequently found adjacent to IDC in *BRCA1/2* mutants compared to sporadic breast cancer cases [20]. Yet recent findings have highlighted that DCIS is routinely identified during prophylactic mastectomy for *BRCA* mutation carriers [21]. Yang et al. [22] illustrated that the majority of *BRCA*-related tumors contained DCIS. A notable concordance rate between the phenotypes of DCIS and IDC components was observed, hinting at a possible DCIS-linked premalignant pathway. Our data corroborate this, with 121 out of 157 patients (77.1%) presenting with DCIS. This high prevalence of concurrently detected DCIS suggests that DCIS might precede invasive carcinoma even in mutation carriers.

The literature proposes that IDC cohabiting with DCIS represents a distinct biological entity relative to IDC in isolation [23]. The prognostic implications of concomitant DCIS are mixed. One analysis associated IDC-DCIS with elevated Ki-67 expression and diminished ER expression, implying a more aggressive nature [15]. Conversely, Mylonas et al. [24] observed reduced expression of HER2 and Ki-67 in IDC-DCIS, signifying a less malignant phenotype. A study from Korea, which assessed 1,751 breast cancer patients, noted that those with DCIS components exhibited higher expression of ER, PR, and HER2. Still, the grade of DCIS proved more critical than its mere presence [25]. Our results specifically address the prognostic role of DCIS in *BRCA1/2*-mutant breast cancer, revealing different features in the IDC-DCIS group, such as association with higher hormone receptor expression rates and lower histological grade. Despite this, when analyzing *BRCA1/2*-positive breast cancer patients collectively, the coexistence of DCIS and IDC did not notably alter recurrence risk. Noteworthily, the subgroup evaluation for *BRCA1* and *BRCA2* unveiled that IDC-DCIS correlated with improved DFS in the *BRCA1* group but was indicative of poorer outcomes in the *BRCA2* cohort. This implies that the prognostic value of DCIS diverges based on the type of *BRCA1* and *BRCA2* mutation.

Table 3. Univariate and multivariate Cox regression analysis of risk factors for recurrence

Variable	Univariate		Multivariate	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Age at diagnosis (yr)				
≥40	Reference		Reference	
<40	2.245 (1.002–5.030)	0.049	2.241 (0.980–5.125)	0.056
Mutation type				
BRCA1	Reference			
BRCA2	1.519 (0.715–3.228)	0.277		
Histologic type				
IDC	Reference			
IDC-DCIS	1.006 (0.435–2.327)	0.989		
BRCA and DCIS component				
*BRCA*1 IDC-DCIS	Reference		Reference	
*BRCA*1 IDC	4.128 (1.162–14.658)	0.028	3.818 (1.053–13.847)	0.042
*BRCA*2 IDC-DCIS	3.234 (1.105–9.466)	0.032	3.582 (1.185–10.829)	0.024
*BRCA*2 IDC	0.735 (0.082–6.580)	0.783	0.683 (0.075–6.231)	0.683
Tumor size (cm)				
≤2	Reference			
>2	1.875 (0.887–3.963)	0.100		
Nodal status				
Positive	Reference			
Negative	0.693 (0.338–1.417)	0.315		
Combined ER status and HER2				
ER+/HER2–	Reference			
ER+/HER2+	1.484 (0.708–3.110)	0.296		
ER–/HER2+	3.352 (0.742–15.134)	0.116		
ER–/HER2–	2.840 (0.366–22.029)	0.318		
Ki-67 (%)				
<14	Reference			
≥14	2.541 (0.680–9.494)	0.166		
Operation method				
Breast-conserving surgery	Reference			
Mastectomy	1.314 (0.654–2.641)	0.444		
Chemotherapy				
Yes	Reference			
No	1.352 (0.519–3.518)	0.537		
Radiation therapy				
Yes	Reference			
No	1.056 (0.474–2.354)	0.894		
Hormone therapy				
Yes	Reference			
No	0.815 (0.420–1.724)	0.653		
Salpingo-oophorectomy				
No	Reference		Reference	
Yes	0.110 (0.048–0.252)	<0.001	0.115 (0.049–0.268)	<0.001

HR, hazard ratio; CI, confidence interval; IDC, invasive ductal carcinoma; DCIS, ductal carcinoma *in situ*; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2.

Risk-reducing salpingo-oophorectomy (RRSO) is heralded as the gold standard for mitigating ovarian cancer risk in *BRCA* mutation carriers [26]. The effects of RRSO on breast cancer risk have been meticulously scrutinized. For those with *BRCA*-related breast cancer undergoing breast-conserving surgery, salpingo-oophorectomy could further diminish the threat of ipsilateral breast tumor recurrence [27]. A diminished risk of contralateral breast cancer post-RRSO in both *BRCA1* and *BRCA2* mutation carriers has been reported [28]. Nonetheless, recent studies have challenged these purported risk reductions [29]. Our research explored predictors for both locoregional and distant recurrence, identifying salpingo-oophorectomy

as a significant determinant. Diagnosis at a younger age also emerged as a noteworthy predictor for recurrence in univariable analysis, as proven by existing literature [30]. These insights underscore the importance of risk-reduction strategies for *BRCA* mutation carriers, particularly in the younger cohorts at augmented risk.

This study is not without limitations. Primarily, it was a single-institution endeavor with a retrospective review of the data. The sample size for certain subgroups was confined owing to the limited number of *BRCA* mutation patients. Additionally, despite claims of no distinct characteristics of *BRCA* mutation-linked breast cancer in Western patients [9], our cohort was exclusively composed of Korean women. Future prospective, multi-center research with more extensive cohorts is imperative to validate and expand on our findings.

In summation, we discerned that DCIS, when accompanying invasive carcinoma, assumes a varied prognostic role in *BRCA1* and *BRCA2* mutation subcategories. *BRCA1/2*-positive breast cancers with DCIS components are inclined to express hormone receptors and exhibit a lesser grade compared to cases with only IDC. Recognizing oophorectomy as a pivotal predictor for diminished recurrence risk accentuates the importance of contemplating this intervention in the management of *BRCA1/2* mutation carriers diagnosed with breast cancer. Furthermore, the correlation between younger age at diagnosis and an escalated recurrence risk emphasizes the necessity for tailored treatment and monitoring protocols for this patient subset.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

ORCID iD

Kyung-Hwak Yoon: https://orcid.org/0000-0002-6206-7767
Eun-Kyu Kim: https://orcid.org/0000-0003-1318-0939
Hee-Chul Shin: https://orcid.org/0000-0001-6512-2218

Author Contribution

Conceptualization, Methodology: HCS
Formal Analysis: KHY
Investigation: KHY, HCS
Project Administration: EKK, HCS
Writing – Original Draft: KHY, HCS
Writing – Review & Editing: All authors

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