Research Article

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The presence of a palpable mass is an independent predictor of microinvasion in Ductal Carcinoma in situ of the Breast

Meme Duktal Karsinoma in situ hastalarında mikroinvazyonun bağımsız bir öngörücüsü olarak palpabl kitle varlığı

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Abstract

Purpose: Breast cancer is the most common cancer among women worldwide. Ductal Carcinoma in situ (DCIS) is one of the most common types of these cancers. Factors associated with microinvasion still need to be investigated.

Materials and methods: In this retrospective study, we analyzed data from 70 female patients diagnosed with DCIS and managed at a tertiary center between 2011 and 2024. Demographic parameters, clinicopathological characteristics, and immunohistochemical findings of the patients were examined in comparison with their microinvasion status.

Results: 70 female patients with Ductal Carcinoma in situ, with a median age of 51 years, were investigated. Among these patients, 17 cases (24.3%) had microinvasion. Compared with demographic parameters, only BMI was associated with microinvasion status. Patients with higher BMI had lower risk of microinvasion (p=0.038). The presence of a palpable mass was significantly higher in patients with microinvasion (p=0.001), suggesting a potential link between tumor palpability and invasion.

Immunohistochemical analysis demonstrated associations between hormone receptor status, HER2 expression, and microinvasion. The presence of HER2 was significantly associated with microinvasion (p=0.026). Multivariate analysis however, revealed that tumor palpability was the only independent factor associated with microinvasion status (Odds Ratio: 5.233; 1.339-20.455; p=0.017).

Conclusion: The presence of a palpable mass emerged as the only independent factor associated with microinvasion in DCIS.

Keywords: DCIS, palpable mass, microinvasion, breast cancer, sentinel iymph node.

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Öz

Amaç: Meme kanseri, Dünya genelinde kadınlar arasında en sık görülen kanser türüdür. Duktal Karsinoma İn Situ (DKIS), bu kanserlerin en yaygın türlerinden biridir. Mikroinvazyonla ilişkili faktörlerin daha fazla araştırılması gerekmektedir.

Gereç ve yöntem: Bu retrospektif çalışmada, 2011-2024 yılları arasında bir üçüncü basamak sağlık merkezinde DKIS tanısı almış ve tedavi edilmiş 70 kadın hastanın verileri analiz edildi. Hastaların demografik parametreleri, klinikopatolojik özellikleri ve immünohistokimyasal bulguları, mikroinvazyon durumlarına göre karşılaştırıldı.

Bulgular: Ortalama yaşı 51 olan 70 kadın hasta incelendi. Bu hastalar arasında 17 vakada (%24,3) mikroinvazyon tespit edildi. Demografik parametreler arasında sadece vücut kitle indeksi (VKİ) mikroinvazyon durumu ile ilişkili bulundu. Daha yüksek VKİ'ye sahip hastalarda mikroinvazyon riski daha düşük olarak saptandı (p=0,038). Mikroinvazyonu olan hastalarda ele gelen kitlenin varlığı anlamlı derecede daha yüksekti (p=0,001). Bu durum, tümörün palpabilitesi ile invazyon arasında potansiyel bir bağlantıyı düşündürmektedir. İmmünohistokimyasal analizler, hormon reseptör durumu, HER2 ekspresyonu ve mikroinvazyon arasında ilişkiler olduğunu ortaya koydu. HER2 varlığı, mikroinvazyon ile anlamlı şekilde ilişkili bulundu (p=0,026). Ancak, çok değişkenli analizler sonucunda, tümör palpabilitesinin mikroinvazyon durumuyla ilişkili tek bağımsız faktör olduğu belirlendi (Odds Ratio: 5,233; 1,339-20,455; p=0,017).

Sonuç: DCIS'de, ele gelen kitlenin varlığı, mikroinvazyonla ilişkili tek bağımsız faktör olarak öne çıkmıştır.

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Anahtar kelimeler: DKIS, palpabl kitle, mikroinvazyon, meme kanseri, sentinel lenf nodu.

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Introduction

Ductal Carcinoma in Situ (DCIS), also referred to as intraductal carcinoma, is a non-invasive breast cancer defined by the proliferation of abnormal epithelial cells confined within the basal membrane. The diagnosis changes to invasive breast cancer when the basal membrane is disrupted, making DCIS a recognized precursor to invasive breast carcinoma.

Breast cancer is the leading cancer type among women globally, with DCIS representing 20-25% of newly diagnosed breast cancers in the United States. The increasing prevalence of DCIS diagnoses parallels the growing use of screening mammography, as a majority of cases are first identified through this method. In contrast, prior to the widespread implementation of mammographic screening, DCIS accounted for less than 5% of newly diagnosed breast cancer cases [1, 2].

DCIS associated with invasive carcinoma measuring ≤1 mm is classified as “DCIS with microinvasion” (DCIS/microinvasion) rather than invasive breast carcinoma. Studies indicate that DCIS with microinvasion accounts for less than 1% of all breast cancers, and the limited number of cases has resulted in an incomplete understanding of its prognostic significance [3].

There are five histopathological subgroups of DCIS: comedo, cribriform, micropapillary, papillary, and solid DCIS. DCIS commonly exhibits a variety of these histopathological structures. Micropapillary, cribriform, and papillary DCIS are considered low-grade lesions, while solid and comedo DCIS are high-grade and show an increased risk of progressing to invasive carcinoma [4].

The treatment of DCIS typically involves a combination of surgery, radiation therapy, and hormone therapy. Treatment decisions are guided by factors such as tumor stage, histopathological findings (including classification, hormone receptor status, and the presence of microinvasion), as these influence recurrence risk. Surgical options for DCIS include breast-conserving surgery (BCS) followed by radiotherapy or mastectomy, with hormone therapy recommended for hormone receptor-positive cases. Both approaches have been shown to provide equivalent long-term survival outcomes. During mastectomy, sentinel lymph node biopsy (SLNB) may be performed to assess axillary metastasis. SLNB is commonly carried out using blue dye (e.g., isosulfan blue) or radioactive colloid [5-7].

High-grade DCIS with large tumors, suspected microinvasion, and solid or cribriform patterns may warrant SLNB. DCIS with microinvasion occurs in 0.68-2.4% of all breast cancer cases and approximately in 14% of DCIS cases. Because DCIS is by definition non-invasive, it is not expected to spread to axillary lymph nodes. Data from the NSABP B24 trials indicate that the rate of axillary recurrence in DCIS, independent of treatment, is 0.36 per 1000 cases. Therefore, SLNB may be deemed unnecessary in DCIS cases [8-11].

Factors potentially associated with microinvasion in DCIS patients include age, tumor size, histopathological features (such as grade, comedonecrosis, ER/PR receptor status, and HER2 expression), and axillary lymph node metastasis. These are also important clinicopathological indicators for breast cancer prognosis [12].

This study explores the relationship between clinical and demographic factors and microinvasion among DCIS patients.

Materials and methods

Approval for the study was obtained from the Pamukkale University Hospital Non-Invasive Clinical Research Ethics Committee (number 18 dated 22/10/2024, E-60116787-020-604967). All stages of the project were conducted in accordance with the Helsinki Declaration. Patient data used in the study were obtained from the University Hospital’s electronic information system and pathology archive. 70 female patients who were treated for

Ductal Carcinoma in situ at the Breast Surgery Clinic between December 2011 and December 2024, and whose data were fully accessible through the hospital's electronic PACS system, were included in the study. The data were reviewed retrospectively. The patients included in the study were evaluated for medical history, sociodemographic data, type of surgical treatment, pathological results of sentinel lymph node biopsy (SLNB), and histopathological features of DCIS (histologic subtype, nuclear grade, presence of comedo necrosis, tumor diameters, histopathological grade, presence of microinvasion, hormone receptor status, HER2 status, Ki-67 proliferation index percentage).

The estrogen receptor (ER) and progesterone receptor (PR) statuses of the patients were determined from immunohistochemistry results, with a value of ≥1% considered positive. The HER2 status was obtained from immunohistochemistry or fluorescence in situ hybridization (FISH) results. Tumors classified as FISH positive with IHC 3+ and IHC 2+ were categorized as HER2 positive; tumors that were FISH negative, IHC 1+, or IHC 2+ were classified as HER2 negative. No experimental studies were conducted. Molecular subtyping was performed according to the latest St. Gallen Consensus in 2013 [13]. The classifications are as follows:

- Luminal A (ER positive, PR >20%, HER2 negative, and Ki-67 index <20%),
- Luminal B/HER2 negative (ER positive, PR <20%, HER2 negative, and Ki-67 index >20%),
- Luminal B/HER2 positive (ER positive, any PR, HER2 positive, and any Ki-67 index),
- HER2 positive (ER negative, PR negative, HER2 positive, and any Ki-67 index),
- Triple negative (ER negative, PR negative, HER2 negative, and any Ki-67 index).

Statistical analysis

Data analysis was conducted using the software SPSS 21.0 (SPSS Inc., Chicago, IL), which was used for the statistical analysis. Continuous variables were assessed for normality using visual inspection and the Shapiro-Wilk test. Variables following a normal distribution were reported as mean (SD), while categorical variables were presented as frequencies and percentages. Normally distributed continuous variables were compared using the Student's t-test, and 95% confidence intervals (CIs) were calculated for differences in means. Differences between categorical variables were evaluated using the Chi-square test. A *p*-value of less than 0.05 was considered statistically significant. Multivariable analysis was conducted using a logistic regression model to evaluate the independent effects of different factors.

Results

Among 70 female Ductal Carcinoma in situ patients, 17 (24.3%) cases had microinvasion. The demographical characteristics of the patients are presented in Table 1. Among these parameters, only BMI was associated with microinvasion status. Patients with higher BMI had a lower risk of microinvasion (p=0.038).

Diagnostic methods and treatment

The study comprised 70 patients, categorized into two groups: those without microinvasion (n=53) and those with microinvasion (n=17).

Tru-cut biopsy was performed on 22 patients (31.4%), evenly distributed between those without microinvasion (n=11) and those with microinvasion (n=11). Excisional biopsy was conducted on 18 patients (25.7%), with 16 patients in the non-microinvasion group and 2 in the microinvasion group. Wire-guided breast biopsy was utilized in 30 patients (42.8%), including 26 without microinvasion and 4 with microinvasion.

Sentinel lymph node biopsy (SLNB) was performed on all 70 patients, with the following results: 67 patients (95.7%) were SLNB-negative, including 51 in the non-microinvasion group and 16 in the microinvasion group. SLNB positivity (1+ nodes) was identified in 2 patients (2.8%), both from the non-microinvasion group, and none in the microinvasion group. SLNB positivity (2+ nodes) was observed in 1 patient (1.4%) from the microinvasion group, with none in the non-microinvasion group. The difference in SLNB outcomes between the groups was not statistically significant (p=0.152).

The surgical methods employed for the 70 patients were categorized based on microinvasion status: those without microinvasion (n=53) and those with microinvasion (n=17). The distribution of procedures was as follows:

- Simple mastectomy was performed in 48 patients (68.5%), including 35 without microinvasion and 13 with microinvasion.
- Breast-conserving surgery was conducted in 12 patients (17.1%), with 11 in the non-microinvasion group and 1 in the microinvasion group.
- Mastectomy with immediate prosthesis was carried out in 6 patients (8.5%), of whom 5 were without microinvasion and 1 with microinvasion.
- Modified radical mastectomy was performed in 4 patients (5.7%), with 2 in each group.

The differences in surgical methods between the groups were not statistically significant (p=0.322) (Table 2).

Table 1. Demographic parameters of Ductal Carcinoma *in situ* Patients with or without Microinvasion

	Total patients (n=70)	Without Microinvasion (n=53)	With Microinvasion (n=17)	*p* value	Test value
Age (years)	51±10.6	51.6 ± 10.4	49.3 ± 11.8	0.445[a]	t=0.768
BMI (kg/m²)	27.5±5.1	28.3±5.3	25.3±4.12	0.038*[a]	t=2.118
Age of menarge	12.7±1.8	12.7±1.16	12.5±3.1	0.655[a]	t=0.449
Number of deliveries	1.9±0.8	2.0±0.8	1.7±0.7	0.202[a]	t=1.290
Age of first pregnancy	23.0±5.4	23.1±5.6	23.1±4.7	0.998[a]	t=-0.003
Breastfeeding history					
No (n=7)	7 (10%)	4 (57.1%)	3 (42.9%)	0.349[b]	X=1.459
Yes (n=63)	63 (90%)	49 (77.8%)	14 (22.2%)		
Breastfeeding duration (months)	21.8±13.8	22.3±14.1	19.9±12.9	0.535[a]	t=0.624
Smoking status					
Nonsmoker	63 (90%)	48 (76.2%)	15 (23.8%)	1.0[b]	X=0.078
Ever smoked	7 (10%)	5 (71.4%)	2 (28.6%)		
Oral contraceptive use					
Never used	59 (84.3%)	44 (74.6%)	15 (25.4%)	1.0[b]	X=0.264
Used	11 (15.7%)	9 (81.8%)	2 (18.2%)		
Menopausal status					
Premenopausal	32 (45.7%)	24 (75.0%)	8 (25.0%)	0.089[b]	X=0.016
Postmenopausal	38 (54.3%)	29 (76.3%)	9 (23.7%)		
Hormone therapy status					
Never used	67 (95.7%)	50 (74.6%)	17 (25.4%)	1.0[b]	X=1.005
Used	3 (4.3%)	3 (5.7%)	0 (0.0%)		

*p<0.05; BMI: Body Mass Index, [a]Student's t-test, [b]Chi-square test; Continuous parameters are presented as mean (standard deviation) categorical parameters are presented in number of cases (percentage of the case)

Table 2. Surgical management in Ductal Carcinoma in situ patients

Surgical Methods	Total patients (n=70)	Without Microinvasion (n=53)	With Microinvasion (n=17)
Simple Mastectomy	48 (68.5%)	35	13
Breast-conserving surgery	12 (17.1%)	11	1
Mastectomy and immediate prosthesis surgery	6 (8.5%)	5	1
Modified radical Mastectomy	4 (5.7%)	2	2

[a]Chi-square test

Clinicopathological characteristics

Clinicopathological features of the patients were compared between the two groups according to their microinvasion status. History of breast cancer, BIRADS category, Paget appearance, tumor diameter, and the quadrant of the tumor were similar among patients with and without microinvasion. However, presence of a palpable mass was associated with microinvasion status (Table 3.) Microinvasion was observed in 46.5% and 9.5% of the cases with and without palpable breast mass, respectively (p=0.001).

Immunohistochemical findings

Immunohistochemical analysis demonstrated associations between hormone receptor status, HER2/neu (Cerb2) expression, and microinvasion. Among these patients, 37 (52.9%) were HER2-negative and 33 (47.1%) were HER2-positive. In the HER2-negative group, 32 patients (86.5%) had no microinvasion, while 5 patients (13.5%) had microinvasion. In the HER2-positive group, 21 patients (63.6%) had no microinvasion, whereas 12 patients (36.4%) had microinvasion. The presence of HER2 was significantly associated with microinvasion (p=0.026) (Table 4).

Table 3. Clinicopathological features of the patients with or without Microinvasion

	Total patients (n=70)	Without Microinvasion (n=53)	With Microinvasion (n=17)	*p* value	Test value
Family history					
No family history	58 (82.9%)	44 (75.9%)	14 (24.1%)	1.000[a]	X=0.004
With family history	12 (17.1%)	9 (75.0%)	3 (25.0%)		
BIRADS mammography result					
0 No family history	9 (12.9%)	8 (88.9%)	1 (11.1%)		
1 With family history	2 (2.9%)	1 (50.0%)	1 (50.0%)		
2	7 (10.0%)	5 (71.4%)	2 (28.6%)	0.348[a]	X=5.590
3	1 (1.4%)	1 (100.0%)	0 (0.0%)		
4	46 (65.7%)	36 (78.3%)	10 (21.7%)		
5	5 (7.1%)	2 (40%)	3 (60.0%)		
Palpable mass					
No	42 (60.0%)	38(90.5%)	4(9.5%)	0.001*[a]	X=12.444
Yes	28(40.0%)	15(53.6%)	13(46.4%)		
Paget appearance					
No	60 (85.7%)	45 (75.0%)	15 (25.0%)	1.000[a]	X=0.117
Yes	10 (14.3%)	8 (80.0%)	2 (20.0%)		
Tumor diameter	14.5±11.1	13.4±9.3	17.8±15.5	0.161[a]	t=-1.418

Table 3. Clinicopathological features of the patients with or without Microinvasion (continued)

Quadrant of the Tumor					
UOQ	48 (68.6%)	34 (70.8%)	14 (29.2%)		
UIQ	9 (12.9%)	9 (100.0%)	0 (0.0%)		
LOQ	5 (7.1%)	3 (60.0%)	2 (40.0%)	0.268[a]	X=5.192
LIQ	3 (4.3%)	3 (100.0%)	0 (0.0%)		
Retroareolar	5 (7.1%)	4 (80.0%)	1 (20.0%)		
Tumor Grade					
1	6 (8.6%)	6 (100.0%)	0 (100.0%)		
2	48 (68.6%)	36 (75.0%)	12 (25.0%)	0.307[a]	X=2.360
3	16 (22.9%)	11 (68.8%)	5 (31.2%)		
Tumor Grade					
≤2	54 (77.1%)	42 (77.8%)	12 (22.2%)	0.513[a]	X=0.547
3	16 (22.9%)	11 (68.8%)	5 (31.2%)		
Multicentricity					
No	48 (68.6%)	36 (75.0%)	12 (25.0%)	0.837[a]	X=0.042
Yes	22 (31.4%)	17 (77.3%)	5 (22.7%)		
Ductal type Without comedo patern	26 37.1%)	17 (65.4%)	9 (34.6%)	0.121[a]	X=2.400
With comedo patern	44 62.9%)	36 (81.8%)	8 (18.2%)		

*p<0.05, [a]Chi-square test; Continuous parameters are presented as mean (standard deviation); categorical parameters are presented in number of cases (percentage of the case); BIRADS: Breast-Imaging Reporting and Data System, UOQ: Upper Outer Quadrant
UIQ: Upper Inner Quadrant, LOQ: Lower Outer Quadrant, LIQ: Lower Inner Quadrant

Table 4. Comparison of Immunhistochemistry results of the patients between Ductal Carcinoma *in situ* Patients with or without Microinvasion

	Total patients (n=70)	**Without Microinvasion (n=53)**	**With Microinvasion (n=17)**	***p* value**	***Test value***
ER					
Negative	17 (24.3%)	11 (64.7%)	6 (35.3%)	0.329[a]	X=1.480
Positive	53 (75.7%)	42 (79.2%)	11 (20.8%)		
PR					
Negative	27 (38.6%)	18 (66.7%)	9 (33.3%)	0.162[a]	X=1.957
Positive	43 (61.4%)	35 (81.4%)	8 (18.6%)		
HER2/neu (Cerb2)					
Negative	37 52.9%	32 86.5%	5 13.5%	0.026*[a]	X=4.953
Positive	33 47.1%	21 63.6%	12 36.4%		
Luminal Type					
Luminal A type	16 (22.9%)	15 (93.8%)	1 (6.2%)		
Luminal B type	37 (52.9%)	27 (73%)	10 (27%)	0.222[a]	X=4.395
Her2/Neu positive	10 (14.3%)	6 (60%)	4 (40%)		
Triple negative	7 (10%)	5 (71.4%)	2 (28.6%)		
Ki 67 staining					
<20 %	33 (47.1%)	26 (78.8%)	7 (21.2%)	0.571[a]	X=0.321
20 %	37 (52.9%)	27 (73%)	10 (27%)		

*p<0.05; ER: Estrogen Receptor, PR: Progesterone Receptor, [a]Chi-square test; Continuous parameters are presented as mean (standard deviation); categorical parameters are presented in number of cases (percentage of the case)

BMI, presence of palpable mass, and Cerb2 status, which are the parameters that were found to be significantly associated with microinvasion in univariate comparison, were analyzed in logistic regression analysis. This analysis revealed that the presence of a palpable mass was the only independent predictor of microinvasion in Ductal Carcinoma in situ of the breast (Odds Ratio:5.233, 95% CI:1.339-20.455, p=0.017) (Table 5).

Table 5. Logistic regression analysis for predicting microinvasion in Ductal Carcinoma *in situ* Patients

Parameters	B	Standard error	Odds ratio	95% confidence interval for the odds ratio	*p* value
Constant	0.114	2.123	1.120		0.957
BMI	-0.100	0.076	0.905	0.780-1.051	0.190
Cerb2 status	0.974	0.672	2.649	0.709-9.891	2.649
Palpable mass	1.655	0.696	5.233	1.339-20.455	0.017*

BMI: Body Mass Index

Discussion

This study analyzed 70 female patients with Ductal Carcinoma in Situ (DCIS), with a median age of 51 years. Microinvasion was identified in 17 patients (24.3%). Univariate analysis showed that BMI, the presence of a palpable mass, and HER2/neu (Cerb2) positivity were associated with microinvasion. However, multivariate analysis identified the presence of a palpable mass as the only independent factor associated with microinvasion.

In DCIS patients, identifying features that help predict prognosis is crucial for determining the appropriate treatment strategy. Microinvasion is associated with a worse prognosis, influencing decisions regarding surgical methods, the need for sentinel lymph node biopsy, and postoperative follow-up. Clinicopathological tests that raise suspicion of microinvasion are particularly valuable in guiding these decisions. Patient demographic data and histopathological evaluations of tumors provide insights into the likelihood of microinvasion. In both DCIS and DCIS-Mi patients, larger tumor size, higher nuclear grade, hormone receptor (HR) negativity, and HER2 overexpression are associated with recurrence and poor prognosis [14].

The findings obtained in our study showed that Her2 positivity and palpable mass increased the risk of microinvasion. In addition, we think that the risk of microinvasion may be lower in patients with higher BMI. However, the factors previously associated with microinvasion in the literature, such as the presence of axillary metastasis, the presence of comedonecrosis, ER, PR negativity, were not found to be significantly related to microinvasion in our study. On the other hand, our results showed that higher BMI was associated with lower microinvasion risk, which this finding, consistent with the literature, shows that larger body size is not associated with known adverse features of DCIS, such as larger tumor size, higher nuclear grade, or the presence of necrosis. In contrast, some studies linked obesity to invasive breast cancer [15, 16]. Our findings interestingly suggest that the presence of a palpable mass is an independent predictor of microinvasion risk in DCIS cases.

In the study conducted by Canbay et al. [17], SLNB positivity was found to be high (5.8%) in pure DCIS cases. The probability of transformation into invasive cancer was found to be higher in patients with SLNB positivity, palpable mass, and tumor diameter >3 cm. When we examined the SLNB results, 4 patients (5.71%) were found to be SLNB-positive, consistent with the findings of Canbay et al. [17] However, this rate is lower than that reported by Diaz Casas et al. [18]. SLNB may be performed as part of surgery in DCIS patients suspected to be at risk for invasive carcinoma.

In a study by Magnoni et al. [19] involving 257 patients with microinvasive Ductal Carcinoma in situ (DCIS) who underwent sentinel lymph node biopsy (SLNB), 226 patients (87.9%) had negative sentinel lymph nodes (SLNs), while 31 patients (12.1%) were found to have metastatic SLNs. After a median follow-up period of 11 years, only one recurrence was observed in the 15 patients with positive SLNs who did not undergo axillary lymph node dissection. No recurrences were reported among the 16 patients with positive SLNs who underwent axillary dissection. In our treatment group, 4 patients (5.7%) underwent modified radical mastectomy, which also includes axillary dissection; 2 of them were in the non-microinvasive group and 2 were in the microinvasive group. In our study, only 3 out of 17 patients with microinvasive DCIS demonstrated SLNB positivity. Although SLNB positivity in DCIS patients was not statistically significant in our findings, based on current literature, we recommend performing SLNB in DCIS patients to assess potential lymph node involvement. SLNB positivity is considered an important indicator of poor prognosis and recurrence risk.

In a study by Champion et al. [20], utilizing a large sample from a national cancer database, it was observed that DCIS with microinvasiveness was more likely to be ER-negative, PR-negative, HER2-positive, and of higher grade compared to invasive breast cancers. These findings suggest that DCIS with microinvasiveness exhibits more aggressive characteristics. In the literature, estrogen and progesterone receptor expression rates in DCIS are reported to range from 60% to 81% [21]. Similarly, in our study, ER expression was found to be 75%, and PR expression was 61%. However, no significant relationship was identified between hormone receptor expression and microinvasion in our study.

HER2 overexpression was identified as the only significant predictor of invasive disease, suggesting that HER2 expression plays a key role in the progression of DCIS lesions to invasive carcinoma [22]. HER2 status in DCIS has been associated with an increased risk of recurrence, with HER2-positive DCIS often presenting as larger lesions. HER2 positivity is also linked to a higher likelihood of progression to invasive carcinoma. In a study by Roses et al. [23], similarly, in our study, HER2 positivity was found to be significantly higher in the DCIS group with microinvasion.

Yu et al. [24] investigated the relationship between molecular subtypes and microinvasion, reporting that tumors were larger and had higher nuclear grades in DCIS patients with microinvasion. They also found that microinvasion rates were lower in luminal-like tumors but higher in ERBB2+ and basal-like DCIS. Similarly, in our study, the risk of microinvasion was significantly increased in the HER2-positive group. However, we did not observe a significant correlation between molecular subtypes and microinvasion, likely due to the relatively small sample size in our study. We believe that subgroup analyses in larger cohorts could provide more robust and meaningful insights.

Upon evaluating histopathological subtypes, comedo carcinoma is reported as the most common histological subtype in DCIS with microinvasion [25]. In our study, the comedo pattern was detected in 62.9% of cases, aligning with the literature, while its detection rate in the microinvasive group was 18.2%. This suggests that, despite being a common subtype, the comedo pattern is not a definitive factor in the relationship with microinvasion.

Maffuz et al. [26] demonstrated in their study that the rate of microinvasion was higher in DCIS patients with tumors larger than 2.5 cm compared to those with smaller tumors. They also reported that such lesions often included various high-grade histological subtypes and were associated with comedonecrosis, palpable masses, and nipple discharge. Similarly, a study by Lagios et al. [27] found that the incidence of microinvasion was 29% in tumors larger than 26 mm, compared to 2% in tumors smaller than 25 mm. However, in our study, we found that the palpability of the mass, rather than its diameter, was independently associated with microinvasion. This may be due to changes in tissue characteristics that occur when microinvasion begins in a sufficiently large tumor, leading to the formation of a palpable mass. Therefore, we believe that the presence of a palpable mass in clinical practice should serve as a warning sign for microinvasion in the management of DCIS patients. DCIS

with microinvasion is biologically more aggressive and carries a higher risk of potential metastatic disease compared to DCIS without microinvasion. Current literature also indicates that disease-free survival rates are longer in patients without a microinvasive component [14]. Thus, close monitoring of patients with DCIS microinvasion, particularly those presenting with a palpable mass as highlighted in our study, is crucial.

In a recent study by Balac et al. [28], which compared the rates of progression to invasive cancer between patients with palpable DCIS and those diagnosed with DCIS through imaging, no significant difference was found between the two groups. Although our study does not focus on the long-term risk of recurrence or progression to invasive cancer, it has shown that patients with palpable DCIS may have a higher likelihood of harboring microinvasion, which is associated with poor prognosis. We believe our findings could contribute to the existing literature on this subject.

The limitations of our study include its retrospective design and the relatively small patient cohort.

In conclusion, this study highlights the complex interplay between demographic, clinicopathological, and immunohistochemical factors in assessing microinvasion risk in DCIS. The observed association between lower BMI and reduced microinvasion risk, along with the significance of HER2 positivity, offers a foundation for targeted risk assessment in DCIS management. Notably, the presence of a palpable mass emerged as the only independent factor associated with microinvasion, suggesting that physical examination may provide valuable prognostic information prior to surgery. Further prospective studies with larger patient cohorts are warranted to confirm these findings.

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Y.A.K. performed the histopathological examinations of the patients. In addition, all authors discussed the entire study and approved the final version.

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