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Upgraded Malignancy from High-Risk and Borderline Breast Lesions: Immunohistochemical and Clinical Characteristics

고위험 및 경계성 유방 병변에서 업그레이드된 악성 종양: 면역조직화학적 및 임상적 특징

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Purpose: The purpose of this study was to investigate the immune-histochemical characteristics of upgraded malignancy from high-risk and borderline breast lesions, and to correlate the upgrade rates with clinical findings.

Materials and Methods: We scrutinized image-guided biopsy records retrospectively, and included all women afflicted with high-risk and borderline breast lesions during the period, 2011 to 2015, inclusive. A total of 340 high-risk and borderline lesions were identified by the pathologist in biopsy samples and thereafter, surgical excision and/or image follow-up for at least 24 months was performed. We compared the clinical emanating from both high-risk and borderline lesions, and with and without cancer upgrade. In the instances of lesions with cancer upgrade, histologic and immuohistochemical reviews were performed.

Results: Of the 340 high-risk or borderline lesions, 18.8% (64/340) were upgraded. The upgrade rates were higher in patients of more advanced age, larger body habitus and afflicted with atypical ductal hyperplasia rather than with other pathology ($p < 0.05$). In the lesions with cancer upgrade ($n = 64$), there was no lymph node metastasis. The estrogen receptor-positive (93.8%), progesterone receptor-positive (87.5%), human epidermal growth factor receptor type 2-negative (90.6%), Ki-67-negative (82.8%), and Luminal A (76.6%) types were seen more frequently.

Conclusion: Most upgraded malignancies arising from high-risk and borderline breast lesions were found to be Luminal A-type with good prognostic factors, and the upgrade rates correlated with clinical characteristics.

Index terms
Image-Guided Biopsy
Breast Neoplasm
Atypical Ductal Hyperplasia
Immunohistochemistry

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INTRODUCTION

Breast cancer is not a single disease entity, but a heterogeneous or a spectrum of disease entity. Evaluation of breast lesions with percutaneous needle biopsy, including ultrasound (US)-guided and stereotactic biopsy, is an established practice at general medical centers (1-3). Percutaneous needle biopsies of complex histologic lesions with a spectrum of benign, atypical and malignant changes can result in upgrade or underestimation of the histopathologic findings at post-procedural surgical excision. Therefore, high-risk and borderline lesions require imaging and pathology correlation to determine whether imaging and pathology show concordance and whether tissue sampling is adequate (4).

So-called high-risk and borderline lesions are breast lesions that have an increased risk of breast cancer development or more sinister pathology around or in association with the lesion. Atypical ductal hyperplasia (ADH), lobular neoplasm (atypical lob-

ular hyperplasia, lobular carcinoma *in situ*) radial scar, papillary neoplasm, flat epithelial atypia (FEA), and mucocele-like lesions are included in high-risk breast lesions (5, 6).

While the majority of high-risk and borderline lesions may require surgical excision given retrospective data for upgrade rates, close observation may be appropriate in certain selected cases (1, 2, 4, 6-9). Furthermore, prospective data are needed to better direct patient care and research focused on immunohistochemical characteristics is needed to advance medicine in breast care.

Therefore, in our study, we investigated the immunohistochemical characteristics of upgraded malignancy from high-risk or borderline breast lesions with the goal of comparing the clinical findings, tumor sizes, and pathologic types between high-risk and borderline lesions without and with cancer upgrade.

MATERIALS AND METHODS

This study was approved by our Institutional Review Board (Seoul St. Mary's Hospital, The Catholic University of Korea, KC16RISI0439). Informed consent was waived for this retrospective study.

Patients and Clinical Findings

From January 2011 to July 2015, we reviewed 9600 image-guided biopsies performed at our institution, including US-guided core needle biopsy and mammography-guided stereotactic vacuum-assisted biopsy. US-guided core needle biopsy was performed using a 14-gauge dual-action semiautomatic core biopsy needle with a 22-mm throw (Stericut with coaxial; TSK Laboratory, Tochigi, Japan). For prone-type mammography-guided stereotactic vacuum-assisted biopsies, the Mammo Test (Siemens AG, Munich, Germany) and Mammotome® (Ethicon Endo-Surgery, Johnson & Johnson, Cincinnati, OH, USA) with an 11-gauge needle were used. We extracted all women with pathologic results of high-risk and borderline lesions, including ADH, lobular neoplasm, radial scar, papillary neoplasm, FEA, and mucocele-like lesions. Of these, 2 cases were excluded from the study due to follow-up loss during surveillance.

Ultimately, a total of 340 (3.5%, 340/9600) high-risk and borderline lesions were identified by the pathologist in biopsy samples and were followed on surveillance for more than 24 months. Of them, 293 patients underwent surgical excision, and 47 patients were followed only by images. From the electronic medical records, age, breast cancer history, the method of detection (mammography or breast US), and biopsy method were analyzed. Lesion size was analyzed by measuring the longest diameter on mammography or breast US.

For lesions upgraded to malignancy, the grade of malignancy was analyzed by pathologic report after surgical excision as low, intermediate, and high for ductal carcinoma *in situ* (DCIS) and well, moderate, and poorly differentiated for invasive carcinoma.

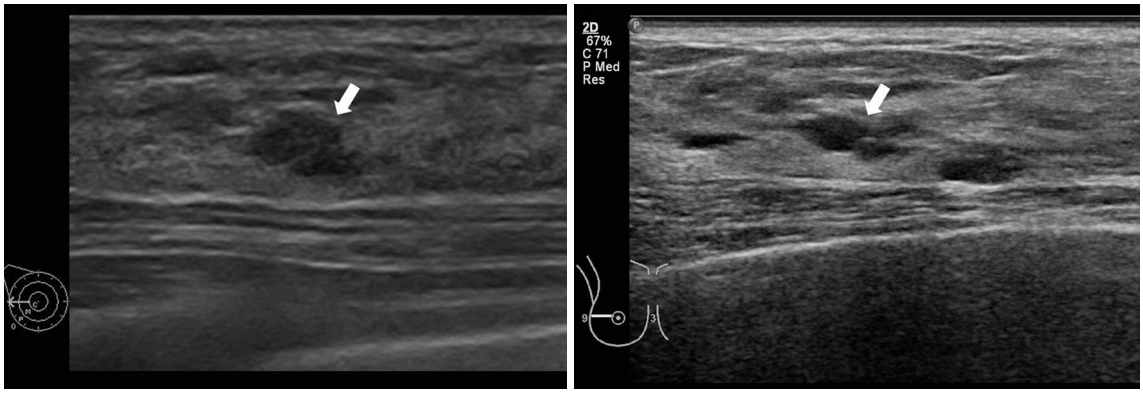
The immunohistochemical analyses were performed with antibodies to estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor type 2 (HER2), Ki-67, and epidermal growth factor receptor (EGFR). Subtypes were classified on the basis of immunohistochemical staining results, including Luminal A [hormone receptor (ER or PR)-positive/negative, low Ki-67 (< 14%)], Luminal B [hormone receptor positive/negative, HER2-positive or HER2-negative & high Ki-67 (≥ 14%)], HER2-positive (hormone receptor-negative, HER2-positive), or basal (hormone receptor- and HER2-negative) (10).

Statistical Analysis

Descriptive statistics are presented as means and standard deviation or percentages of participants. The association between the status of cancer upgrade and baseline variables were assessed by univariable and multivariable logistic regression analysis. Sub-group analysis of cancer upgrading status and biopsy pathology were assessed by chi-square test or Fisher's exact test. Analyses were performed with the use of SAS software, version 9.4 (SAS Institute Inc., Cary, NC, USA) and MedCalc version 12.7 (MedCalc Software, Mariakerke, Belgium). Two-sided $p < 0.05$ was considered statistically significant.

RESULTS

The histopathologic results of the total of 340 lesions were as follows: 37.6% (128/340) were ADH, 3.2% (11/340) were lobular neoplasms, 12.6% (43/340) were radical scars, 27.1% (92/340) were papillary neoplasms, 6.5% (22/340) were FEAs, and 12.9% (44/340) were mucocele-like lesions. All forty-seven lesions (13.8%, 47/340) that were followed were stable during radiologic follow-up for more than 24 months, including 6 ADHs, 1



A B

Fig. 1. Imaging findings of a 36-year-old woman who had a papillary neoplasm by US-guided core needle biopsy that was not surgically confirmed.
A. On the US, there was a 0.6-cm-sized oval hypoechoic mass with microlobulated margins at 9 o'clock in the right breast, which was thought to be Breast Imaging Reporting and Data System category 4A (arrow).
B. On the follow-up US after 5 years, the lesion had not changed (arrow).
US = ultrasound

lobular neoplasm, 13 radial scars, 8 papillary neoplasms (Fig. 1), 6 FEAs, and 13 mucocele-like lesions. Two hundred ninety-three lesions (86.2%, 293/340) underwent surgical excision, including 122 ADHs, 10 lobular neoplasias, 30 radial scars, 84 papillary neoplasms, 16 FEAs, and 31 mucocele-like lesions. Of them, 81.2% (276/340) were not upgraded, and 18.8% (64/340) were upgraded; 13.5% (46/340) were upgraded to DCIS, and 5.3% (18/340) were upgraded to invasive cancer (Fig. 2). Table 1 demonstrated that cancer upgrade was significantly more likely occur with older age, larger tumor size, and pathologic types. In contrast, there were no differences in breast cancer history, detection image modality (mammography vs. US), and biopsy method.

Mean age was significantly different between patients without and with cancer upgrade [46.76 ± 10.82 years old and 50.14 ± 10.03, respectively ($p < 0.05$); DCIS (48.83 ± 10.15 years old) and invasive cancer (53.50 ± 9.15 years old)]. Tumor size was also a significant risk factor for cancer upgrade. The mean tumor sizes were as follows: without cancer upgrade, 1.26 ± 1.35 cm; with cancer upgrade, 2.17 ± 2.28 ($p < 0.05$); DCIS, 2.25 ± 2.37 cm; and invasive cancer, 1.95 ± 2.09 cm. Univariable and multivariate analysis (Table 2) demonstrated that cancer upgrade was significantly more likely occur with larger tumor size and with ADH than with radial scar or mucocele-like lesion ($p < 0.05$).

Of the 128 ADHs, 31 lesions were upgraded to malignancy (24 DCIS, 7 invasive carcinoma), and 97 lesions were not upgraded. Of the 11 lobular neoplasms, 2 lesions were upgraded to malignancy (all invasive carcinoma), and 9 lesions were not upgraded. Of the 43 radial scars, 3 lesions were upgraded to malignancy (1 DCIS, 2 invasive carcinoma), and 40 lesions were not upgraded. Of the 92 papillary neoplasms, 21 lesions were upgraded to malignancy (16 DCIS, 5 invasive carcinoma), and 71 lesions were not upgraded. Of the 22 FEAs, 4 lesions were upgraded to malignancy (all DCIS), and 18 lesions were not upgraded. Of the 44 mucocele-like lesions, 3 lesions were upgraded to malignancy (1 DCIS, 2 invasive carcinomas), and 41 lesions were not upgraded.

The characteristics of 64 cases of upgraded malignancy are summarized in Table 3. In the surgically proven malignancies, the grades of DCIS and invasive cancers were evaluated. There were no cases accompanying lymph node metastasis (0%). In two upgraded malignancies from ADH, there were missing data in ER, PR, HER2, Ki-67, EGRF, and subtype. ER-positive (93.8%, 60/62), PR-positive (87.5%, 56/62), HER2-negative (90.6%, 58/62), Ki-67-negative (82.8%, 53/62), and EGFR-negative (84.4%, 54/62) cases were more frequent. According to immunohistochemical definitions, Luminal A (76.6%, 49/62) was most frequent, followed by Luminal B (17.2%, 11/62), HER2-positive (1.6%, 1/62), basal type triple-negative (1.6%, 1/62), and non-basal type triple-negative (0%).

DISCUSSION

There are several studies assessing the correlations between

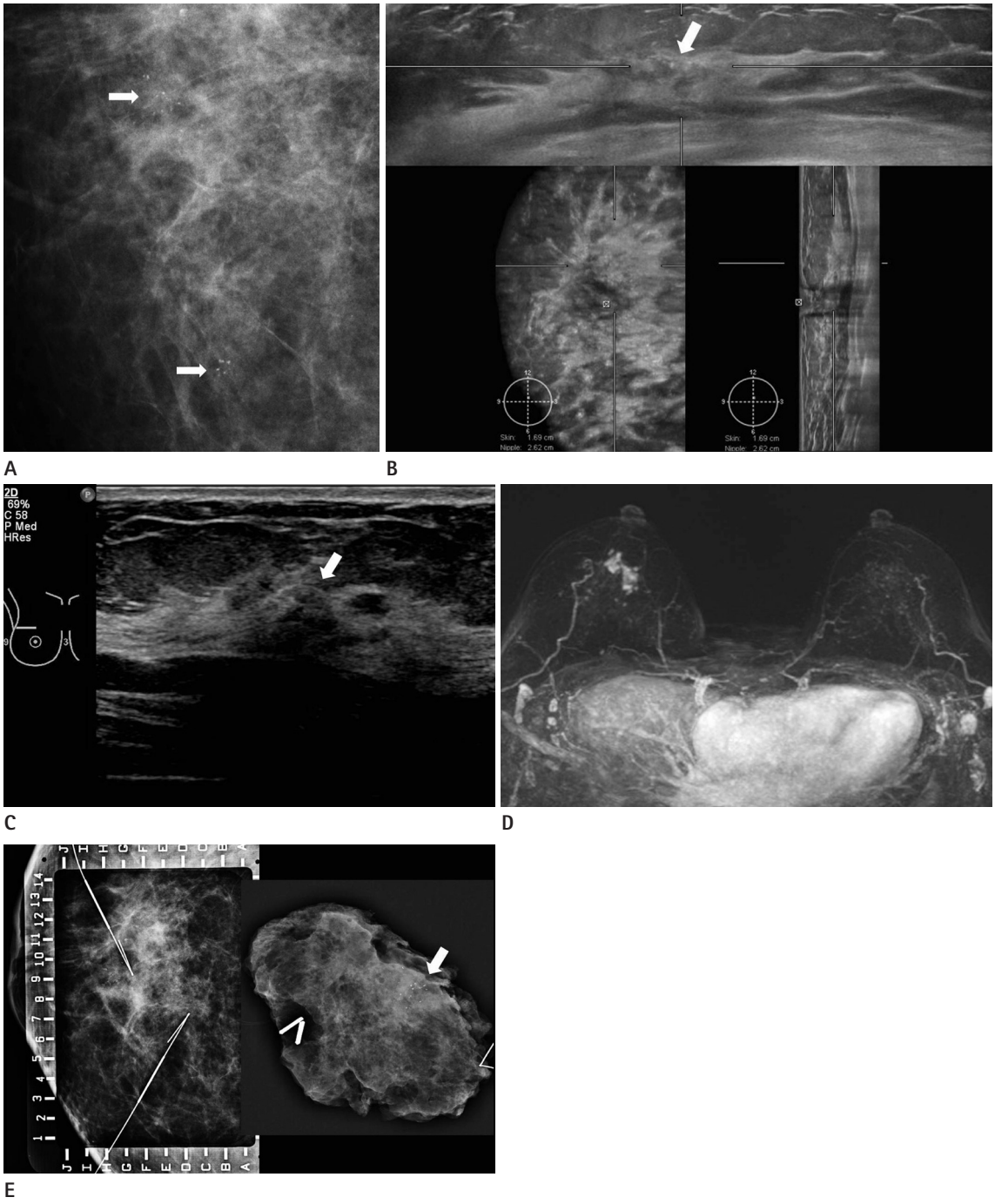


Fig. 2. Imaging findings of a 56-year-old woman who had an ADH by US-guided core needle biopsy; it was upgraded to invasive ductal carcinoma after surgical excision. The immunohistochemical characteristics of this case were Luminal A [estrogen receptor (+), progesterone receptor (+), human epidermal growth factor receptor type 2 (-), Ki- 67 (low), epidermal growth factor receptor (-)].
A. Right magnification view shows two areas of grouped amorphous microcalcifications in the middle and inner upper portions of the right breast, which were thought to be Breast Imaging Reporting and Data System category 4B (arrows).
B, C. By both automated **(B)** and hand-held ultrasound **(C)**, there was an irregular isoechoic mass with suspicious calcifications at 12 o'clock in the right breast, which correlated with a prior mammography (arrows). Through US-guided core needle biopsy, the lesion was confirmed as ADH.
D. On the maximal intensity projection image of breast magnetic resonance imaging, there was a regional nonmass enhancement 2.6 × 1.5 cm in size at 12 o'clock in the right breast.
E. The patient underwent mammography-guided localization and surgical excision. The specimen contained microcalcifications approximately 4 cm in extent (arrow) and was confirmed as invasive ductal carcinoma.
ADH = atypical ductal hyperplasia, US = ultrasound

Table 1. Clinical Characteristics and Pathology Results of High Risk and Borderline Lesions

	Without Cancer Upgrade	With Cancer Upgrade	Cancer Upgrade (DCIS)	Cancer Upgrade (Invasive Cancer)	*p*-Value*
Number (%)	276 (81.2)	64 (18.8)	46 (13.5)	18 (5.3)	
Age (year)	46.76 ± 10.82	50.14 ± 10.03	48.83 ± 10.15	53.50 ± 9.15	0.023
Size (cm)	1.26 ± 1.35	2.17 ± 2.28	2.25 ± 2.37	1.95 ± 2.09	< 0.001
Biopsy method					0.705
MSVAB	34 (10.0)	9 (2.6)	8 (2.4)	1 (0.3)	
UCNB	242 (71.2)	55 (16.2)	38 (11.2)	17 (5.0)	
Breast cancer history					0.839
Negative	244 (71.8)	56 (16.5)	40 (11.8)	16 (4.7)	
Positive	32 (9.4)	8 (2.4)	6 (1.8)	2 (0.6)	
Mammo detection					0.251
Negative	164 (48.2)	33 (9.7)	24 (7.1)	9 (2.6)	
Positive	112 (32.9)	31 (9.1)	22 (6.5)	9 (2.6)	
USG detection					0.205
Negative	35 (10.3)	12 (3.5)	11 (3.2)	1 (0.3)	
Positive	241 (70.9)	52 (15.3)	35 (10.3)	17 (5.0)	
Biopsy pathology					0.027
ADH	97 (28.5)	31 (9.1)	24 (7.1)	7 (2.1)	
Lobular neoplasm	9 (2.7)	2 (0.6)	0 (0)	2 (0.6)	
Radial scar	40 (11.8)	3 (0.9)	1 (0.3)	2 (0.6)	
Papillary neoplasm	71 (20.9)	21 (6.2)	16 (4.7)	5 (1.5)	
Flat epithelial atypia	18 (5.3)	4 (1.2)	4 (1.2)	0 (0)	
Mucocele-like lesion	41 (12.1)	3 (0.9)	1 (0.3)	2 (0.6)	

Continuous variables are expressed as mean ± standard deviation, and categorical variables are expressed as number (percentage).
*Between the 'without cancer upgrade' and 'with cancer upgrade' groups.
ADH = atypical ductal hyperplasia, DCIS = ductal carcinoma *in situ*, Mammo = mammography, MSVAB = mammography-guided stereotactic vacuum-assisted biopsy, UCNB = ultrasound-guided core needle biopsy, USG = ultrasonography

Table 2. Univariable and Multivariate Model of High Risk and Borderline Lesions to Upgrade Breast Cancer

	Univariable		Multivariate	
	Odds ratio (95% CI)	*p*-Value	Odds ratio (95% CI)	*p*-Value
Age (> 40)	2.117 (0.995–4.502)	0.052		
Size (cm)		0.003		0.014
1 ≤	1 (reference)		1 (reference)	
1–2	1.28 (0.65–2.53)	0.478	1.17 (0.57–2.32)	0.654
> 2	3.24 (1.64–6.41)	0.001	2.83 (1.38–5.75)	0.004
Biopsy method	0.86 (0.39–1.89)	0.706		
Breast cancer history	1.09 (0.48–2.49)	0.840		
Mammo detection	1.38 (0.80–2.38)	0.252		
USG detection	0.63 (0.31–1.29)	0.208		
Biopsy pathology		0.070		0.125
ADH	1 (reference)		1 (reference)	
Lobular neoplasm	0.70 (0.14–3.39)	0.653	0.80 (0.12–3.43)	0.789
Radial scar	0.24 (0.07–0.81)	0.022	0.31 (0.07–0.94)	0.065
Papillary neoplasm	0.93 (0.49–1.74)	0.811	1.11 (0.57–2.14)	0.753
Flat epithelial atypia	0.70 (0.22–2.21)	0.538	0.75 (0.20–2.23)	0.624
Mucocele-like lesion	0.23 (0.07–0.79)	0.020	0.26 (0.06–0.78)	0.033

Age is included for multivariate logistic regression model whether *p*-value is statistically significant or not.
ADH = atypical ductal hyperplasia, CI = confidence interval, Mammo = mammography, USG = ultrasonography

Table 3. Histopathologic and Molecular Characteristics of Upgraded Cancers from High-Risk and Borderline Lesions

	Initial Biopsy Result, *n* (%)						
	ADH (*n* = 31)*	Lobular (*n* = 2)	Radial (*n* = 3)	Papillary (*n* = 21)	Flat (*n* = 4)	Mucocele (*n* = 3)	Total (*n* = 64)*
Type of cancer							
DCIS	24 (77.4)	0 (0)	1 (33.3)	16 (76.2)	4 (100)	1 (33.3)	46 (71.9)
Invasive cancer	7 (22.6)	2 (100)	2 (66.7)	5 (23.8)	0 (0)	2 (66.7)	18 (28.1)
DCIS grade							
Low	9 (37.5)	0 (0)	1 (100)	7 (43.8)	3 (75)	0 (0)	20 (43.5)
Intermediate	12 (50)	0 (0)	0 (0)	8 (50)	0 (0)	1 (100)	21 (45.7)
High	3 (12.5)	0 (0)	0 (0)	1 (6.3)	1 (25)	0 (0)	5 (10.9)
Invasive cancer grade							
Well differentiated	2 (28.6)	1 (50)	0 (0)	1 (20)	0 (0)	2 (100)	6 (33.3)
Moderately differentiated	5 (71.4)	1 (50)	2 (100)	4 (80)	0 (0)	0 (0)	12 (66.7)
Poorly differentiated	0 (0.0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
ER							
Negative	1 (3.2)	0 (0)	0 (0)	1 (4.8)	0 (0)	0 (0)	2 (3.1)
Positive	28 (90.3)	2 (100)	3 (100)	20 (95.2)	4 (100)	3 (100)	60 (93.8)
PR							
Negative	1 (3.2)	0 (0)	1 (33.3)	4 (19)	0 (0)	0 (0)	6 (9.4)
Positive	28 (90.3)	2 (100)	2 (66.7)	17 (81)	4 (100)	3 (100)	56 (87.5)
HER2							
Negative	29 (93.5)	2 (100)	2 (66.7)	18 (85.7)	4 (100)	3 (100)	58 (90.6)
Positive	0 (0)	0 (0)	1 (33.3)	3 (14.3)	0 (0)	0 (0)	4 (6.3)
Ki-67							
Negative	22 (71.0)	2 (100)	3 (100)	19 (90.5)	4 (100)	3 (100)	53 (82.8)
Positive	7 (22.6)	0 (0)	0 (0)	2 (9.5)	0 (0)	0 (0)	9 (14.1)
EGFR							
Negative	26 (83.9)	2 (100)	2 (66.7)	19 (90.5)	3 (75)	2 (66.7)	54 (84.4)
Positive	3 (9.7)	0 (0)	1 (33.3)	2 (9.5)	1 (25)	1 (33.3)	8 (12.5)
Subtype							
Luminal A	22 (71)	2 (100)	2 (66.7)	16 (76.2)	4 (100)	3 (100)	49 (76.6)
Luminal B	6 (19.4)	0 (0)	1 (33.3)	4 (19)	0 (0)	0 (0)	11 (17.2)
HER2+	0 (0)	0 (0)	0 (0)	1 (4.8)	0 (0)	0 (0)	1 (1.6)
Triple-(basal like)	1 (3.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.6)

*Two missing data for ER, PR, HER2, Ki-67, EGFR, and subtype in the ADH group.
ADH = atypical ductal hyperplasia, DCIS = ductal carcinoma *in situ*, EGFR = epidermal growth factor receptor, ER = estrogen receptor, HER2 = human epidermal growth factor receptor type 2, PR = progesterone receptor

various imaging findings for breast cancer diagnosis, including mammography, US, and magnetic resonance imaging, along with the clinical features and immunohistopathological markers (11-13). In this study, we focused on investigating the immuohistochemical characteristics of upgraded malignancy from high-risk and borderline lesions and to correlate the upgrade rates with clinical findings.

According to the results of this study, cancer upgrade was significantly more likely occur with older age, larger tumor size, and pathologic types. The biopsy type (US-guided or stereotactic vacuum-associated biopsy) and lesion detection method did not affect the malignancy upgrade rate. These results are consistent with other studies (1, 14).

Rethinking the standard for DCIS treatment is the current research trend (15). There are many papers that distinguish prognosis or analysis of DCIS, an early cancer without invasion, from invasive ductal carcinoma (IDC) (3, 15, 16). In this study, we also analyzed the cases that were upgraded to DCIS and IDC. In the study of Menes et al. (3), most of the women with ADH on needle biopsy who were upgraded to cancer were found to have DCIS (82%, 101/123). More than half (56%, 10/18) of the women with lobular neoplasms who were upgraded to cancer

were found to have invasive carcinoma. Most women had low-grade cancer and low rates of lymph node involvement. These results are consistent with our study. In our study, most of the women with ADH on needle biopsy who were upgraded to cancer were found to have DCIS (77.4%, 24/31). All of the women with lobular neoplasms who were upgraded to cancer were found to have invasive carcinoma. Most cases upgraded to DCIS were low to intermediate grade (89.1%, 41/46), most invasive cancers were well to moderately differentiated (100.0%, 18/18), and no women had lymph node involvement (0%).

The current model of breast cancer is known as a stepwise progression of precursor lesions with cellular atypia into carcinoma in situ and invasive carcinoma (3, 17, 18). The early precursor lesions show relatively few somatic chromosomal alterations, including low-grade DCIS and low-grade invasive carcinoma. In contrast, high-grade lesions, such as high-grade DCIS, show quite different molecular characteristics, such as amplification of the HER2 gene or, less frequently, p53 mutations (3, 12, 15-17). In this study, the most frequent upgraded malignancy from high-risk and borderline lesions was the Luminal A immunohistochemical type of breast cancer 76.6% (49/62) of total upgraded cancers; 71% (22/29) of upgraded cancers from ADH, 100% (2/2) of upgraded cancers from lobular neoplasias, 66.7% (2/3) of upgraded cancers from radial scars, 76.2% (16/21) of upgraded cancers from papillary lesions, 100% (4/4) of upgraded cancers from flat epithelial lesions, and 100% (3/3) of upgraded cancers from mucocele-like lesions. The second most common subtype is the luminal B type [17.2% (11/62) of total]. The HER2-positive and triple-negative subtypes each comprised 1.6% (1/62) of the upgraded cancers. The majority were Luminal subtypes of positive hormone receptors and negative HER2 amplification. This result is thought to be consistent with the model and suggests that high-risk and borderline breast lesions may be in a state of development into low-grade breast cancer with good prognosis (6, 19, 20).

With the development of biochemical science, precision medicine has emerged over the past decade and has changed the nature of therapies in patients with several types of cancers. Breast cancers are also newly classified into several subtypes according to combinations of molecular and cellular analyses, and categorized therapies, such as molecular target therapy, are expected to apply to the biomedical profile of a particular patient's disease (17, 21, 22).

This study had several limitations. First, this is a retrospective study; therefore, it may be affected by selection bias. Second, the population is relatively small and included mixed indications for biopsy, heterogeneous pathologic types and surgery.

In conclusion, the cancer upgrade rates from high-risk and borderline breast lesions were higher in patients with older age, larger lesion sizes, and ADH. Most upgraded malignancies showed the Luminal A immunohistochemical type with good prognosis; lymph node metastasis was rare.

Acknowledgments

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고위험 및 경계성 유방 병변에서 업그레이드된 악성 종양: 면역조직화학적 및 임상적 특징

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목적: 이 연구의 목적은 고위험 및 경계성 유방 병변에서 업그레이드된 악성 종양의 면역조직화학적 특성을 조사하고 임상 소견과 암으로의 업그레이드율의 연관성을 알아보는 데 있다.

대상과 방법: 저자들은 영상유도하 생검 기록을 후향적으로 검토했으며 2011년부터 2015년까지 고위험과 경계성 유방 병변이 있는 모든 여성을 대상으로 하였다. 생검 샘플에서 병리학자에 의해 총 340개의 고위험 및 경계성 병변이 확인되었으며, 수술적 절제 혹은 24개월 이상 추적 검사가 시행되었다. 고위험 및 경계성 병변이 암으로 업그레이드된 경우와 아닌 경우의 임상 소견을 비교하였다. 암으로 업그레이드된 경우에 대하여, 병리조직학적 및 면역조직화학적 검사를 시행하였다.

결과: 340예의 고위험 또는 경계성 병변 중, 18.8%(64/340)가 암으로 업그레이드되었다. 업그레이드율은 고령의 환자, 크기가 큰 병변에서 더 높았고, 다른 병리학적 유형보다 atypical ductal hyperplasia에서 더 높았다($p < 0.05$). 업그레이드된 악성 종양($n = 64$)에서는 림프절 전이가 없었다. Estrogen receptor 양성(93.8%), progesterone receptor 양성(87.5%), human epidermal growth factor receptor type 2 음성(90.6%), Ki-67 음성(82.8%), Luminal A (76.6%)형이 가장 흔하였다.

결론: 고위험 및 경계성 유방 병변에서 업그레이드된 악성 종양은 주로 Luminal A 면역조직화학형과 좋은 예후 인자를 가지며 업그레이드율은 임상 특성과 관련이 있다.

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