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Original Article

Prediction of Oncotype DX Recurrence Score Using Clinicopathological Variables in Estrogen Receptor-Positive/Human Epidermal Growth Factor Receptor 2-Negative Breast Cancer

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Conflict of Interest
The authors declare that they have no competing interests.

ABSTRACT

Purpose: Oncotype DX (ODX) is a well-validated multigene assay that is increasingly used in Korean clinical practice. This study aimed to develop a clinicopathological prediction (CPP) model for the ODX recurrence scores (RSs).
Methods: A total of 297 patients (study group, n = 175; external validation group, n = 122) with estrogen receptor-positive, human epidermal growth factor receptor 2 (HER2)-negative, T1-3N0-1M0 breast cancer, and available ODX test results were included in the study. Risk categorization as determined by ODX RSs concurred with the TAILORx study (low-risk, RS ≤ 25; high-risk, RS > 25). Univariate and multivariate logistic regression analyses were used to assess the relationships between clinicopathological variables and risk stratified by the ODX RSs. A CPP model was constructed based on regression coefficients (β values) for clinicopathological variables significant by multivariate regression analysis.
Results: Progesterone receptor (PR) negativity, high Ki-67 index, and nuclear grade (NG) 3 independently predicted high-risk RS, and these variables were used to construct the CPP model. The C-index, which represented the discriminatory ability of our CPP model for predicting a high-risk RS, was 0.915 (95% confidence interval [CI], 0.859–0.971). When the CPP model was applied to the external validation group, the C-index was 0.926 (95% CI, 0.873–0.978).
Conclusion: Our CPP model based on PR, Ki-67 index, and NG could aid in the selection of patients with breast cancer requiring an ODX test.

Keywords: Breast Neoplasms; Drug Therapy; Ki-67 Antigen; Receptors, Progesterone; Recurrence

INTRODUCTION

Breast cancer is currently the most common cancer worldwide [1]. Over several decades, new drug regimens and treatment strategies have been developed to improve breast cancer cure rates; however, heterogeneous outcomes are problematic when clinicians consider the

Author Contributions

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merits and demerits of chemotherapy, especially in node-negative and estrogen receptor (ER)-positive breast cancer. Pathologists can help clinicians decide the therapeutic options for patients with breast cancer by providing information on pT, pN, lymphovascular invasion (LVI), hormone receptors, and human epidermal growth factor receptor 2 (HER2) status.

Patients with ER-positive breast cancer receive hormonal therapy and usually have a good prognosis; however, some patients, even those with surgically well-treated early-stage cancer, have a progressive clinical course. Thus, the selection of these patients and administration of preemptive chemotherapy before recurrence are becoming important. Commercially available multigene assays provide prognostic and therapy-predictive information on patients with ER-positive, HER2-negative, and node-negative breast cancer [2]. Among them, the Oncotype DX® (ODX) (Genomic Health, Redwood City, USA) test is preferred by the National Comprehensive Cancer Network (NCCN) breast cancer panel for node-negative breast cancer [3]. This assay analyzes the expression of 16 breast cancer-related genes and five reference genes in formalin-fixed, paraffin-embedded tumor tissues using a reverse transcription polymerase chain reaction-based assay and provides results as numerical recurrence scores (RSs) ranging from 0 to 100. Furthermore, RS is predictive of recurrence-free survival and chemotherapy benefit [4-7]. The Trial Assigning Individualized Options for Treatment (TAILORx) demonstrated the ability of ODX to identify patients with early breast cancer who may be exempted from adjuvant chemotherapy [8].

Despite its clinical usefulness, the high cost (~$4,000) of ODX testing, when not covered by health insurance, is an obstacle to its widespread adoption. In addition, testing is more difficult for non-USA residents because of the distance from ODX-performing laboratories and the time required to transport cancer tissues. Because of these obstacles, many researchers have tried to utilize clinicopathological parameters described in surgical pathology reports as surrogates for ODX test results. It has been suggested that a nomogram or scoring system based on tumor size, grade, hormone receptor, and Ki-67 status could be used to predict high- or low-risk ODX RS [9-19]. Although the Ki-67 index has prognostic and predictive value in breast cancer [20], it has rarely been used to predict ODX results, owing to poor inter-observer reproducibility. Since the International Ki-67 Working Group (IKWG) published its recommendations for Ki-67 evaluation in 2011, international multicenter studies have been conducted to establish a standardized counting method [21,22]. Recently, digital image analysis systems have been increasingly used for Ki-67 scoring in South Korea.

In this study, we investigated the association between ODX RSs and clinicopathological variables, including the Ki-67 index, to develop a clinicopathological prediction (CPP) model for ODX RSs.

METHODS

Two hundred and ninety-seven patients with ER-positive, HER2-negative, T1-3N0-1M0 breast cancer and an available ODX test result were included. All patients underwent curative surgery either at the Yeungnam University Hospital (study group, n = 175) or Keimyung University Dongsan Hospital (external validation group, n = 122) between August 2019 and November 2022. Baseline clinicopathological data (age at diagnosis, tumor size, histological grade [HG], nuclear grade [NG], histological type, LVI, axillary lymph node status, and Ki-67 labeling index) were collected from the pathology reports. Immunohistochemical staining for ER (SP1; Ventana

Medical Systems, Tucson, USA), progesterone receptor (PR) (1E2; Ventana Medical Systems), HER2 (4B5; Ventana Medical Systems), and Ki-67 (30-9; Ventana Medical Systems) was performed routinely using the automated Benchmark® platform (Ventana Medical Systems) at the time of diagnosis and interpreted according to the recently published guidelines [21,23,24]. Tumors were considered positive for ER or PR if they showed nuclear staining in more than 1% of the tumor cells. For equivocal HER2 IHC results, the presence or absence of gene amplification was routinely confirmed by *in situ* hybridization using an INFORM® HER2 DNA probe (Ventana Medical Systems). Ki-67 results were expressed as percentages of positively stained cells among all tumor cells by counting at least 1000 invasive cancer cells using iScan Coreo/Virtuoso version 5.6 (Ventana Medical Systems) and GenASIs HiPath™ (Applied Spectral Imaging Ltd., Carlsbad, USA) in the study and validation groups, respectively. ODX RSs were obtained from ODX test reports, and cases were classified as low risk (RS 0–25) or high risk (RS 26–100) in accordance with the TAILORx clinical trial results [8].

χ^2 and *t*-tests were used to compare clinicopathological variables between the low- and high-risk ODX groups. Our goal was to develop a predictive model for risk stratification by the ODX RSs based on clinicopathological variables. Univariate logistic regression was used to assess the relationship between clinicopathological variables and risk stratified by ODX RS. Factors significant in the univariate analysis were utilized in the multivariate logistic regression analysis to construct an ODX risk prediction model (CPP model). To assess model performance, ODX RSs were plotted against the model-predicted risk (from 0 to 1). The ability of the CPP model to differentiate between low-risk and high-risk groups was assessed using a receiver operating characteristic (ROC) curve. The concordance index (C-index) with a 95% confidence interval (CI), as determined by the area under the ROC curve, represents the probability of concordance between the predicted and observed results, which can range from 0.5 (random selection) to 1 (perfect concordance) [11]. Statistical analysis was performed using SPSS version 27.0, for Windows (IBM, Armonk, USA), and *p*-values < 0.05 were considered statistically significant.

This study was approved by the Institutional Review Boards of Yeungnam University Hospital (YUH2022-01-006-002) and Keimyung University Dongsan Hospital (DSMC2022-07-019), and the requirement for informed consent was waived.

RESULTS

Patient characteristics

The clinicopathological characteristics of the study and external validation groups are summarized in **Table 1**. All patients were women with a mean age of 53 years (median, 52, range 27–84). In the study group, 129 patients (73.7%) belonged to the low-risk group based on the ODX RSs, and the remaining 46 (26.3%) patients were classified as high-risk. In the external validation group, 100 (82%) patients had low-risk ODX RS, and 22 (18%) had high-risk RS.

Comparison of clinicopathological factors in the low- and high-risk ODX groups

In the study group, patients in the high-risk group were more likely to be older (> 50 years) ($p = 0.045$), exhibit LVI ($p = 0.043$), have high HG and NG (both $p < 0.001$), be negative for PR expression ($p < 0.001$), and have a high Ki-67 index ($p < 0.001$) when compared with patients in the low-risk group. However, tumor size and lymph node status were not related to risk stratification using ODX RSs (**Table 2**).

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Table 1. Characteristics in the study and external validation groups

Clinicopathologic variables	Study group (n = 175)	External validation group (n = 122)
Age (yr)		
≤ 50	83 (47.4)	48 (39.3)
> 50	92 (52.6)	74 (60.7)
Tumor size (cm)		
≤ 2	113 (64.6)	83 (68)
> 2	62 (35.4)	39 (32)
LN metastasis		
Absent	150 (85.7)	108 (88.5)
Present	25 (14.3)	14 (11.5)
LVI		
Absent	102 (58.3)	95 (77.9)
Present	73 (41.7)	27 (22.1)
Nuclear grade		
1	22 (12.6)	3 (2.5)
2	85 (48.6)	44 (36.1)
3	68 (38.9)	75 (61.5)
Histologic grade		
1	50 (28.6)	15 (12.3)
2	66 (37.7)	44 (36.1)
3	59 (33.7)	63 (51.6)
PR expression		
Positive	152 (86.9)	110 (90.2)
Negative	23 (13.1)	12 (9.8)
Ki-67 expression		
Mean ± SD (%)	17.4 ± 16	21.6 ± 16

Values are presented as number (%).
LN = lymph node; LVI = lymphovascular invasion; PR = progesterone receptor; SD = standard deviation.

Table 2. Comparison of clinicopathological variables in the low- and high-risk groups according to Oncotype DX test results in the study group

Clinicopathological variables	Low-risk (RS ≤ 25) (n = 129)	High-risk (RS > 25) (n = 46)	*p*-value
Age (yr)			0.045
≤ 50	67 (51.9)	16 (34.8)	
> 50	62 (48.1)	30 (65.2)	
Tumor size (cm)			0.409
≤ 2	81 (62.8)	32 (69.6)	
> 2	48 (37.2)	14 (30.4)	
LN metastasis			0.08
Absent	107 (82.9)	43 (93.5)	
Present (mic)	22 (17.1)	3 (6.5)	
LVI			0.043
Absent	81 (62.8)	21 (45.7)	
Present	48 (37.2)	25 (54.3)	
Nuclear grade			< 0.001
1	20 (15.5)	2 (4.3)	
2	77 (59.7)	8 (17.4)	
3	32 (24.8)	36 (78.3)	
Histologic grade			< 0.001
1	47 (36.4)	3 (6.5)	
2	56 (43.4)	10 (21.7)	
3	26 (20.2)	33 (71.7)	
PR expression			< 0.001
Positive	123 (95.3)	29 (63)	
Negative	6 (4.7)	17 (37)	
Ki-67 expression			< 0.001
Mean ± SD (%)	12.8 ± 11.1	30.3 ± 20.2	

RS = recurrence score; LN = lymph node; LVI = lymphovascular invasion; PR = progesterone receptor; SD = standard deviation.

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Table 3. Univariate and multivariate analysis results for predicting patients in the high-risk group (recurrence score > 25) as determined by the Oncotype DX test in the study group

Clinicopathological variables	Univariate analysis			Multivariate analysis		
	Odd ratio	95% CI	*p*-value	Odd ratio	95% CI	*p*-value
Age (yr)			0.047			NS
≤ 50	1					
> 50	2.026	1.008–4.073		-		
Tumor size (cm)			0.41			
≤ 2	1					
> 2	0.738	0.358–1.52		-		
LN metastasis			0.092			
Absent	1					
Present	0.339	0.097–1.193		-		
LVI			0.045			NS
Absent	1					
Present	2.009	1.017–3.97				
Histologic grade			< 0.001			NS
1&2	1					
3	10.056	4.644–21.776				
Nuclear grade			< 0.001			0.001
1&2	1			1		
3	10.912	4.871–24.445		6.932	2.28–21.077	
PR expression			< 0.001			< 0.001
Positive	1			1		
Negative	12.017	4.356–33.155		37.44		
Ki-67 (%)			< 0.001			< 0.001
(continuous)	1.076	1.046–1.105		1.077	1.039–1.116	

CI = confidence interval; NS = not significant; LN = lymph node; LVI = lymphovascular invasion; PR = progesterone receptor.

Factors associated with high-risk ODX RS

The univariate logistic regression analysis revealed that age, LVI, HG, NG, PR status, and Ki-67 index were associated with high-risk ODX test results (**Table 3**). Tumor size and lymph node status were not associated with ODX risk. Multivariate logistic regression analyses, which included six variables that were significant by univariate analysis, showed that NG (p = 0.001), PR status (p < 0.001), and Ki-67 index (p < 0.001) independently predicted ODX risk.

Performance of the CPP model and external validation

A positive correlation was observed between the ODX RS and predicted risk, as determined by multivariate analysis (CPP model) (r = 0.7, p < 0.001) (**Figure 1**). The discriminatory ability of our CPP model to predict high-risk ODX RSs was determined using ROC analysis (**Figure 2A**). The c-index was 0.915 (95% CI, 0.859–0.971), indicating strong predictive ability.

To externally validate our CPP model, an automatic calculator was created using Microsoft Excel to obtain probabilities (%) of high-risk ODX RSs. The calculation was based on regression coefficients (β values) of three variables (1.936 for NG, 3.623 for PR, and 0.074 for Ki-67 index) and a logistic regression constant (−4.714). This tool allows the user to obtain the probability of a high-risk RS for individuals by inputting values for NG (grade 1 or 2 = 0, grade 3 = 1), PR status (positive = 0, negative = 1), and Ki-67 index (%).

The equation was as follows:

$$\frac{\mathrm{EXP}\{(0.074 \times \text{Ki-67}) + (3.623 \times \text{PR}) + (1.936 \times \text{NG}) - 4.714\} \times 100}{1 + \mathrm{EXP}\{(0.074 \times \text{Ki-67}) + (3.623 \times \text{PR}) + (1.936 \times \text{NG}) - 4.714\}}$$

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External validation was performed using a cohort of 122 patients to determine the reproducibility and generalizability of our CPP model. A ROC curve was plotted (**Figure 2B**), and the C-index in the validation group was 0.926 (95% CI, 0.873–0.978), indicating a strong predictive ability.

When 6% was used as the cutoff, 80 (97.6%) of 82 patients with a probability of ≤ 6% had low-risk RS. The ODX RSs of the other two patients were 26 and 28. The positive predictive

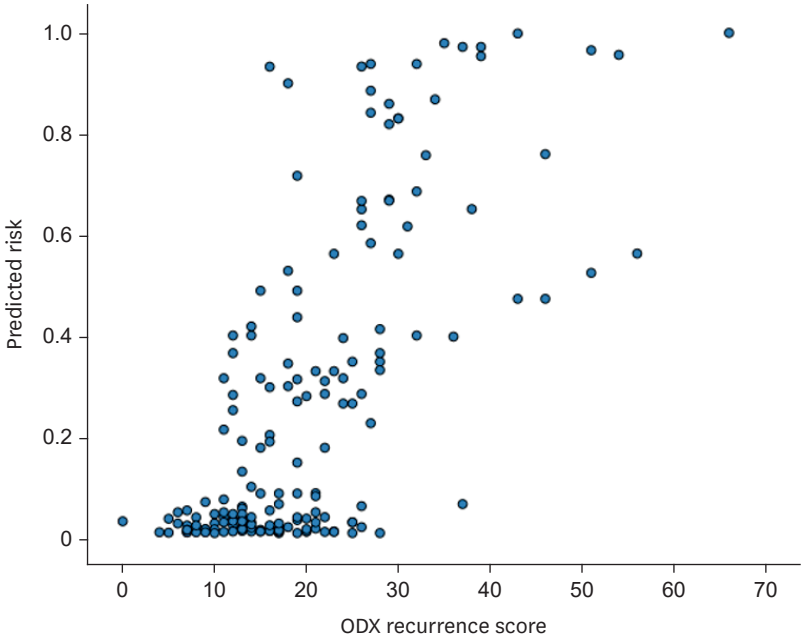

Figure 1. Comparison of predicted risk scores as determined by the multivariate clinicopathological prediction model and Oncotype DX recurrence scores in the study group.
ODX = Oncotype DX.

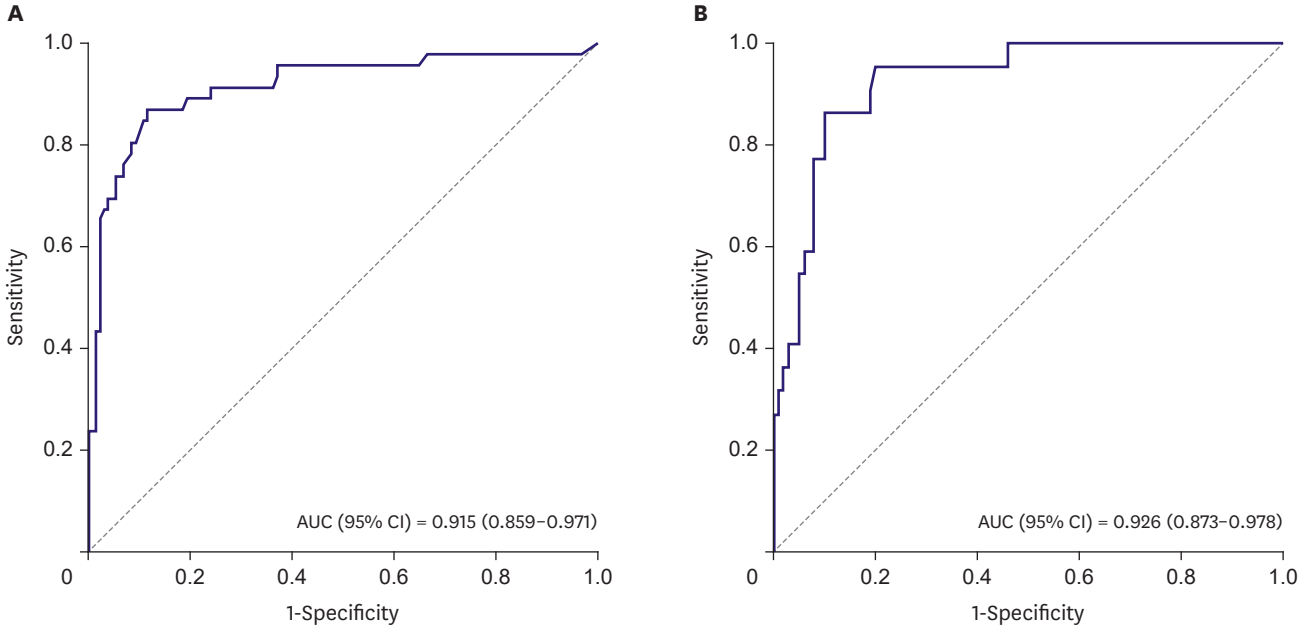

Figure 2. Receiver operating characteristic curve of the clinicopathological prediction model in the (A) study and (B) external validation groups.
AUC = area under the curve; CI = confidence interval.

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value (PPV) for low-risk RS was 98%, and the specificity was 96%. When the same cut-off was applied to the external validation group, the PPV and specificity were 100% (**Table 4**). Using 90% as the cut-off, the PPV for high-risk RS was 92%, specificity was 99% in the study group, and the corresponding values in the validation group were 80% and 98%, respectively.

Validation of the representative nomograms

Our CPP model was compared with three previously published nomograms [12,13,17] used to predict ODX RSs (**Table 5**). As shown in **Table 5**, tumor grade (histologic or nuclear) and PR were included in all studies. In addition, Ki-67 was included in Korean studies and our study but not in Western studies (Tennessee nomogram). The predictive scores and risk probabilities of individuals in our cohort were calculated using an on-line calculator (https://

Table 4. Comparisons of observed risks as determined by the Oncotype DX test and risks predicted by the clinicopathological prediction model in the study and external validation groups

Risk prediction	Study group				External validation group			
	All patients (n = 175)		> 50 yr (n = 92)		All patients (n = 122)		> 50 yr (n = 74)	
	RS ≤ 25	RS > 25	RS ≤ 25	RS > 25	RS ≤ 25	RS > 25	RS ≤ 25	RS > 25
High-risk probability (%)								
≤ 6	80	2	39	1	38	0	19	0
> 6	49	44	23	29	62	22	41	14
	Low-risk	High-risk	Low-risk	High-risk	Low-risk	High-risk	Low-risk	High-risk
Sensitivity	62%		63%		38%		32%	
Specificity	96%		97%		100%		100%	
PPV	98%		98%		100%		100%	
NPV	47%		56%		26%		26%	
High-risk probability (%)								
≤ 90	128	35	62	21	98	14	59	9
> 90	1	11	0	9	2	8	1	5
	Low-risk	High-risk	Low-risk	High-risk	Low-risk	High-risk	Low-risk	High-risk
Sensitivity		24%		30%		36%		36%
Specificity		99%		100%		98%		98%
PPV		92%		100%		80%		83%
NPV		79%		75%		88%		87%

RS = recurrence score; PPV = positive predictive value; NPV = negative predictive value.

Table 5. Comparison of selected previous studies and current study that used clinicopathological variables to predict Oncotype DX test results

Comparison factors	Qrucevic et al. (2019) [12]	Lee et al. (2019) [13]	Yoo et al. (2020) [17]	Current study
Patients	Western	Korean	Korean	Korean
Training group	65,754	340	191	175
Validation group	18,585	145	264	122
Clinicopathological variables includes in prediction model	Tumor size (mm) Tumor grade PR (negative or positive) Histologic type Age (yr)	LVI (present or absent) PR (Allred score) ER (Allred score) Nuclear grade (1, 2 or 3) Ki-67 (%)	Nuclear grade (1–2 or 3) PR (negative or positive) Ki-67 (%)	Nuclear grade (1–2 or 3) PR (negative or positive) Ki-67 (%)
ODX RS cutoff values	≤ 25 (LR), > 25 (HR)	≤ 25 (LR), > 25 (HR)	≤ 25 (LR), > 25 (HR)	≤ 25 (LR), > 25 (HR)
Discrimination (C-index or AUC, 95% CI)				
Training group	0.81 (0.80–0.81)	0.90 (0.85–0.96)	0.856 (0.772–0.939)	0.915 (0.859–0.971)
Validation group	0.812 (0.803–0.822)	0.88 (0.83–0.95)	0.828 (0.757–0.899)	0.926 (0.873–0.978)
External validation with our dataset (n = 297)	0.831 (0.78–0.883)	0.919 (0.877–0.96)	0.899 (0.856–0.942)	-
Predictive ability for correct categorization of a HR or a LR ODX result	Probability for a HR ODX RS ≥ 85% vs. observed HR	Probability for a LR ODX RS ≥ 97% vs. observed LR	Not provided	Probability for a HR ODX RS ≤ 6% vs. observed LR
Sensitivity	14%	50%	-	62%
Specificity	99.9%	95%	-	96%
PPV	94.3%	98%	-	98%
NPV	92.6%	27%	-	47%

LVI = lymphovascular invasion; PR = progesterone receptor; ER = estrogen receptor; ODX = Oncotype DX; RS = recurrence score; LR = low-risk; HR = high-risk; AUC = area under the curve; CI = confidence interval; PPV = positive predictive value; NPV = negative predictive value.

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utgsm.shinyapps.io/OncotypeDXCalculator/) [12] and a Microsoft Excel Worksheet provided by the authors of the study [13], or calculated directly in the nomogram [17]. The C-indices obtained in our cohort were slightly higher than those reported in previous studies.

DISCUSSION

The ODX test was developed for ER-positive breast cancer, and is currently one of the most commonly used genomic assays worldwide. The NCCN, the American Joint Commission on Cancer, and the American Society of Clinical Oncology endorsed the ODX as a test for selecting patients with hormone receptor-positive breast cancer for adjuvant chemotherapy [4,6-8]. Despite its usefulness, ODX testing in countries outside the United States is limited by its high cost and difficulties in transport to suitable laboratories. Institution-based studies have been conducted to predict ODX RSs using clinicopathological variables available from pathology reports [9-11,13,14,16-19]. However, most of these studies were restricted to a limited number of patients. Furthermore, Western populations were used in most studies, and only two were based on the Korean population [13,17].

Allison et al. proposed a simple algorithm for selecting patients for ODX testing using Nottingham grade (HG), PR status, and the Ki-67 index [16]. In their study, HG 1, a high PR, and a low Ki-67 (≤ 10%) indicated a low RS, and conversely, HG 3, a low PR, and a high Ki-67 indicated a high RS. Therefore, they suggested that these subsets of patients may not require ODX testing. Kim et al. used ER, PR, Ki-67, HER2, and Elston grade to develop a nomogram [25]. Random forest and linear regression were used for modeling, and the model was found to safely predict low- or high-risk ODX RS in more than half of the cases with > 95% confidence. Eaton et al. [11] used ER, PR, tumor size, NG, and HG to estimate a simplified risk score. Thibodeau et al. [14] only used HG and PR (GR-PR scores).

Orucevic et al. [12,15] used age, histological type, tumor size, HR, and PR to predict the ODX results in the largest cohort study performed to date (80,000 patients) (Tennessee nomogram). Although studies have shown that ODX RSs are unaffected by ethnicity [26,27], Kim et al. [28] validated the Tennessee nomogram in Korean patients and reported that its C-index was much lower than that reported in a Western population. Therefore, it was concluded that the nomogram cannot be applied to Asian patients. Yoo et al. [17] reported that high NG, no PR expression, and high Ki-67 were associated with a high-risk ODX group; thus, they proposed a nomogram that included these variables to predict high-risk RSs in Korean patients with breast cancer. In another Korean study, Lee et al. [13] developed a nomogram by integrating five prognostic factors (ER, PR, NG, LVI, and Ki-67) to define the low ODX RS subgroup. Our results are consistent with those of previous studies conducted in Korea. The C-index of our CPP model was higher than that of similar studies; however, the number of patients included was lower. We recommend further validation of our CPP model and Korean nomograms using large datasets. We validated the Tennessee nomogram and two of the above-mentioned Korean nomograms in our cohort. The C-indices obtained in our cohort were slightly higher than those reported in previous studies [12,13,17], indicating that the nomograms worked well for different cohorts and ethnicities.

Most nomograms and our model were developed by comparing patients with high-risk ODX RSs (> 25) and those with low-risk ODX RSs (≤ 25). Patients with intermediate-risk ODX RS (11–25) were included in the low-risk group. Although the TAILORx study reported the

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benefit of chemotherapy in patients under 50 years of age with an RS of 16-25, it is unclear whether this was due to the ovarian suppression effects induced by chemotherapy [8]. Thus, premenopausal patients with an RS of 16–25 remained in the gray area when deciding on adjuvant chemotherapy. The NCCN recommends adjuvant endocrine therapy with or without ovarian suppression/ablation or adjuvant chemotherapy followed by endocrine therapy for these patients [3].

PR is an essential variable for predicting ODX RS, and low or no PR expression is associated with high ODX RS [11-14,16-19,25,29]. PR is a potent prognostic factor for ER-positive breast cancer [30-32]. PR expression is linked to functional ER because it is the end product of estrogen activity [33]. An *in vitro* study using MCF-7 cells showed that estrogen-independent PR expression hindered estrogen-associated proliferation [34]. Furthermore, aberrant growth factor pathways such as HER2, insulin-like growth factor-1, and PI3K-AKT-mTOR can downregulate PR expression [35]. These findings support the importance of PR when analyzing risk factors for ER-positive breast cancer.

NG is one of the components consisting of HG, which includes tubule formation, NG, and mitotic count. NG and HG were significant variables associated with high-risk ODX RSs in the univariate analysis; however, unlike NG, HG was not an independent variable in the multivariate analysis. This seems to be due to the strong association between the Ki-67 index and mitotic count, a component of HG. Although it is difficult to accurately evaluate HG in a limited specimen such as a core needle biopsy, NG can be evaluated with a small sample volume.

Although the Ki-67 index has a prognostic value in breast cancer, there are reproducibility issues with this evaluation method. Nevertheless, the Ki-67 index has been used in several studies to estimate the ODX RS using clinicopathological variables; however, the measurement method has not been precisely described [9,13,16,29]. Paik et al. reported that Ki-67 indices measured using an automatic analysis program might act as surrogates for ODX RSs [36]. To minimize the reproducibility problem, we measured the Ki-67 index using an image analysis program and followed the recommendations of the IKWG [21].

This study had several limitations. First, although we included all patients who underwent ODX testing during the study period, the study was limited by its retrospective nature and the small number of patients included. In addition, case selection bias may have influenced the results because not all patients with ER-positive, HER2-negative, T1-3N0-1M0 breast cancer underwent ODX testing for cost reasons. Second, our CPP model applies to patients whose Ki-67 results are expressed as percentage values and can be validated in breast cancer cohorts using Ki-67 indices measured according to the IKWG guidelines [21]. Recently, more institutions have adopted image analysis programs to measure Ki-67 indices. For the Ki-67 index to be a clinically useful marker, all institutions that perform Ki-67 tests should follow the IKWG recommendations.

In conclusion, we developed a CPP model based on PR, NG, and Ki-67 indices to predict high-risk ODX RSs. This model could aid in the identification of patients with breast cancer who require an ODX test. However, further validation of our CPP model using a large data set is required before its clinical application.

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