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ORIGINAL PAPER

Personalized Breast Cancer Prognosis Using a Model Based on MRI and Clinicopathological Variables

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Abstract

This study aimed to develop and internally validate a prognostic prediction model based on MRI, pathological, and clinical findings to predict breast cancer recurrence and death. A retrospective study prediction model was developed using data from 922 breast cancer patients recruited in Duke University Hospital from January 2000 to March 2014. Cox and binary logistic regressions were implemented for hazard score and 2-, 3-, 5-, and 8-year survivals and recurrences. After assessing the collinearity of predictors, both univariable and multivariable analyses were performed. Qualitative and quantitative MRI variables were selected based on clinical expert opinion and literature review. Bootstrap and leave-one-out methods were used for internal validation. Calibration, shrinkage, time-dependent receiver operating characteristic (ROC) curve, and decision-curve analyses were also performed. Finally, a user-friendly calculator was built. Of included participants, 62 (6.72%) died with a mean patient-year follow-up of 8.89 years (CI = 8.74 to 9.04), while 90 (9.76%) experienced recurrence with mean patient-year follow-up of 8.20 years (CI = 7.92 to 8.48). The Akaike information criterion (AIC) value of survival and recurrence models were 752.9 and 1020.7, indicating a good balance between model complexity and fit. Validation model adjusted area under curve (AUC) in 8-, 5-, 3-, and 2-year survivals were 0.740 (CI = 0.711 to 0.768), 0.741 (CI = 0.712 to 0.770), 0.788 (CI = 0.761 to 0.816), and 0.783 (CI = 0.755 to 0.809), while in 8-, 5-, and 3-year recurrences were 0.678 (CI = 0.647 to 0.708), 0.696 (CI = 0.664 to 0.727), and 0.769 (CI = 0.740 to 0.798), respectively. Good calibration and shrinkage parameters were achieved. The internal validation and decision curve analyses highlighted the usefulness of the model across all probability levels. The combined MRI-pathological-clinical model has excellent performance in predicting overall survival and recurrence of breast cancer and may have a role to play in daily personalized breast cancer therapy.

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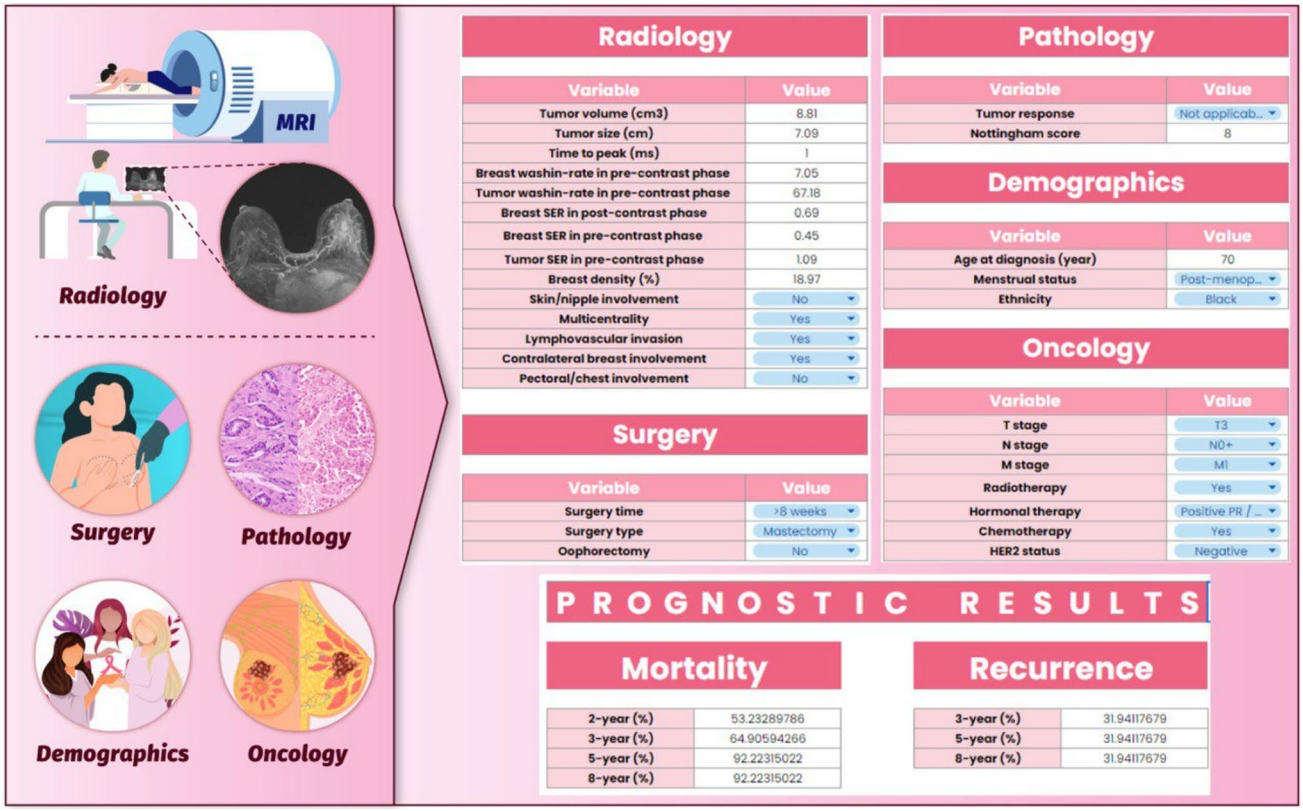
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Graphical Abstract



Keywords Magnetic resonance imaging (MRI) · Breast cancer · Prediction model · Prognostic model study

Introduction

Breast cancer is the most prevalent type of cancer among women, with almost two million cases diagnosed annually [1]. Approximately 6,500,000 individuals died of breast cancer in 2018, according to the Globocan report; this accounted for 6.6% of all cancer-related fatalities, making breast cancer the second most lethal cancer [2]. The prognosis of breast cancer patients and their treatment approach varies substantially depending on the stage of the disease at the time of diagnosis [3]. Several factors have been identified as being linked to recurrence-free survival and are frequently utilized to inform treatment decisions. These factors include clinical variables like age, pathological markers such as estrogen receptor status, and, more recently, genomic markers like the Oncotype DX recurrence score [4]. Historically, imaging modalities such as mammography and ultrasound have been primarily used for diagnosis. However, their role in treatment planning was initially limited to defining the extent of disease. Recent studies have shown that imaging, particularly magnetic resonance imaging (MRI), plays a critical role in guiding surgical decisions and predicting outcomes by providing detailed information on tumor characteristics and extent [3, 4].

Given its current application in diagnosing breast tumor stage and aggressiveness, MRI offers an unprecedented capability to assess breast anatomy in three dimensions [5]. It has been demonstrated that the response of primary breast tumors to neoadjuvant chemotherapy can be more correctly evaluated by dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) compared to clinical examination, mammography, or ultrasound [6]. Furthermore, a recent study found that preoperative MRI features predicted recurrence-free survival better than clinical breast examination, pathological tumor size, and number of involved lymph nodes. Specifically, MRI tumor volume was revealed to be the strongest predictor of recurrence-free survival [7]. By utilizing quantitative data from standard clinical breast MR imaging, such as the signal enhancement ratio and percent enhancement [8], DCE-MRI can accurately determine tumor size, differentiate between scar tissue and recurring cancer, and is the recommended screening method for women with a higher genetic predisposition to breast cancer. These guidelines have been validated by the National Comprehensive

Cancer Network (NCCN) and the American Cancer Society [9].

Few studies evaluated the potential of breast MRI in determining the prognosis of breast cancer patients in prediction model format [10–14]. Hence, in this retrospective study, we developed and internally validated a prognostic prediction model to assess whether MRI parameters (both quantitative and qualitative), in combination with other clinical factors—including pathological, oncological, surgical, reproductive, and physical exam findings—could predict overall survival and recurrence in breast cancer patients. Moreover, we investigated the relationship between the prediction model and prognosis outcomes in breast cancer patients to guide clinical decision-making.

Materials and Methods

The protocol of this study has been registered a priori at https://osf.io/m874w/ (see Appendix A) on the Open Science Framework (OSF) platform. As for reporting, we adhered to Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) reporting guidelines (see Appendix B). The local institutional review board approved the study, and all participants provided written informed consent. Participants were retrospectively enrolled from the Duke-Breast-Cancer-MRI dataset available in the cancer imaging archive (TCIA) gathered in Duke University Hospital [10].

Study Design and Patient Selection

A total of 1150 consecutive female patients with histopathologically confirmed invasive breast cancer underwent preoperative MRI at Duke University Hospital from January 2000 to March 2014 without prior history of breast cancer diagnosis or treatment. A total of 228 patients were excluded based on the following criteria: (1) incomplete pathological or medical records; (2) T1 sequences that were not fat-saturated; (3) sagittal MRIs; (4) missing fat-saturated pre/post-contrast sequence, unclear MRI tags and discordant number of slices; (5) reader not marking any abnormalities or mismarks them; and (6) software failure in image reading or pre-processing (Fig. 1). Finally, 922 patients were included in the study.

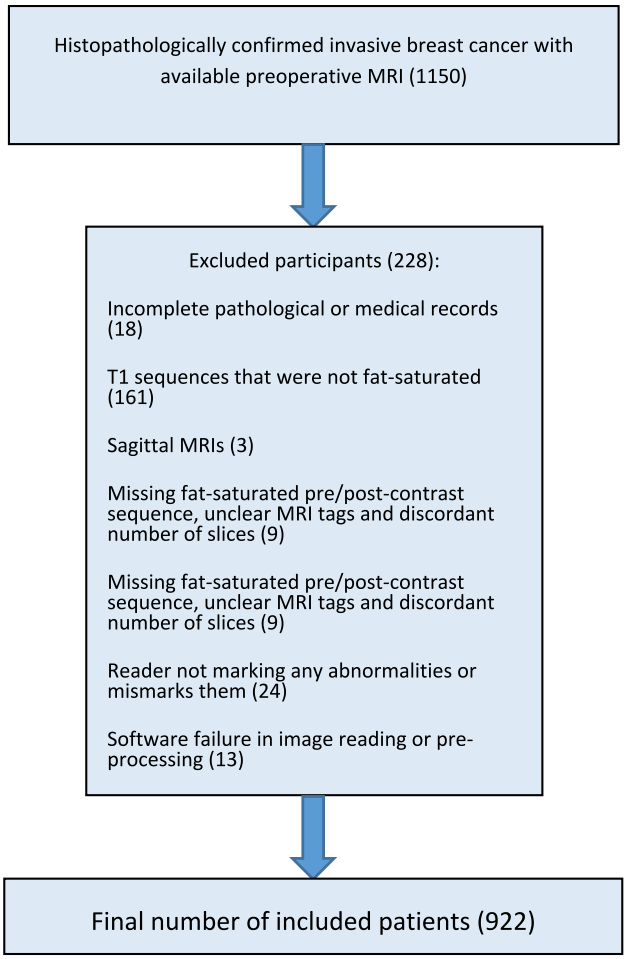


Fig. 1 Flowchart detailing patient inclusion and exclusion criteria

Non-imaging Data Collection

Detailed demographic information was collected, including age (measured in years), race, and menopause. The race was divided into three layers: white, black, and others. The third layer was used as the reference for race (meaning Asian, Native American, Hispanic, Multiethnic, Hawaiian, and American Indian ethnicities). The menopausal status was defined as premenopause and postmenopause. The reference layer was the premenopausal status at the time of diagnosis. In case of potential information loss, we determined menopausal status using the 51-year-old cutoff age as the prevailing mean menopausal age in the USA.

Pathology results were reviewed for the ER, PR, and HER2 status. For all these, the negative status was defined as the reference layer. As for TNM staging, T status was defined as an ordinal variable with four layers, with T1 being the reference layer. The N component was defined as N0 vs. N0 + levels, with N0 as the reference layer. Patients without regional lymph node involvement were considered N0, and those with involvement of one or more regional lymph nodes were considered N0 +. Also, patients were categorized as without distant metastasis (M0) or with distant metastasis (M1), with M0 being the reference layer. The Nottingham score was also included in the predictor list (range = 3–9). In the absence of data for TNM staging status or Nottingham score, the worst-case scenario was presumed to exist (i.e.,

T4, N0 +, M1, and Nottingham score of 9) based on the need to ensure a conservative approach in outcome risk assessment as well as enhancing clinical utility by simulating the real clinical context. Furthermore, the surgical procedures of patients were categorized qualitatively through three modes: surgery not performed, lumpectomy, and mastectomy, with the first one being defined as the reference layer. Also, we categorized surgical timing based on the time elapsed between diagnosis and surgery. Early surgery was defined as surgery being performed within 56 days of the diagnosis date (reference layer). Conversely, surgery performed after 56 days or not performed at all was classified as late surgery. This definition was chosen to reflect the recommended timeframe (56 days) for surgery to maximize survival benefits while allowing sufficient time for necessary preoperative evaluations and preparations [3, 6].

Radiation therapy, chemotherapy, hormone therapy, and anti-HER2 therapy were evaluated qualitatively, and each treatment modality was dichotomized as either "not received" (reference layer) or "received" (administered either before or after surgery). The pathological response of tumors to neoadjuvant therapy was classified into three modes: no neoadjuvant therapy administered (reference layer), complete response, and incomplete response. Finally, oophorectomy status was categorized into two groups: no oophorectomy (reference layer) and receiving therapeutic or prophylactic oophorectomy.

Imaging Data Collection

Breast axial MRIs were obtained for the patients enrolled in our research using 1.5 T or 3 T scanners, while they were in the prone position. Information pertaining to the scanner and the parameters for MR acquisition are presented in Appendix C. The data was annotated in two subsets consisting of 271 and 651 patients, with variations in the procedure. For the first group, a team of six fellowship-trained radiologists independently reviewed their assigned studies. Each radiologist used a graphical user interface to create three-dimensional bounding boxes around up to five lesions (both masses and non-mass enhancements). For the second subset of 651 patients, a panel of four fellowship-trained radiologists was implemented. The subsetting process was adopted to balance the need for accurate annotations with the practical constraints of processing a large dataset. This approach allowed for a detailed and comprehensive annotation process, essential for establishing a robust baseline for our model. All examiners of outcome variables (including radiologists) were blinded to relevant predictors. Also, predictor variable evaluators were blinded to both outcome variables and other predictors [10]. If the patient had undergone multiple biopsies, the biopsied tumor was identified after reviewing relevant radiology and pathology reports. If there were multiple biopsies, the largest one was selected for further analysis. In this modified approach, radiologists were provided with the biopsy location(s) and instructed to annotate the largest biopsied lesion. Similar to the first phase, each radiologist independently reviewed their assigned studies. However, unlike the prior phase, radiologists in this group had access to the picture archiving and communication system (PACS) for additional reference, if needed.

In the evaluation of qualitative MRI parameters, five bimodal predictors of tumor multifocality/multicentrality, contralateral breast involvement, lymphovascular invasion, skin/nipple involvement, and chest/pectoral involvement were included, and the negative status of each was defined for reference layer. Also, the radiological response of tumors to neoadjuvant therapy was classified into three modes: no neoadjuvant therapy administered (reference layer), complete response, and incomplete response.

From the 529 quantitative MRI parameters, tumor size (i.e., tumor major axis measured in cm), tumor volume (measured in cm^3), breast non-tumor volume in T1-weighted pre-contrast phase (calculated as non-tumoral breast tissue volume divided by the total breast volume measured in percentage), mean tumoral signal-to-noise ratio (SER), mean peritumoral SER in pre-contrast T1, mean peritumoral SER in post-contrast T1, mean tumoral wash-in rate (defined as maximum slop between the time of contrast inflow and time of peak intensity), mean peritumoral SER in pre-contrast T1, mean peritumoral SER in post-contrast T1, time to peak (time taken for contrast enhancement to reach its peak intensity which is measured in ms), and ratio of breast tissue being enhanced more than 70% in T1-weighted pre-contrast phase were selected as potential predictors. We also deliberately excluded genetic parameters and advanced imaging techniques like PET/CT and PET/MRI to make model more suitable for implementation in developing countries where these resources might be scarce [10].

Methodology and Statistical Analysis

The statistical analyses were conducted using Stata 17, SPSS 27, and Medcalc 22.017. Predictor selection was mainly based on their ease of use, clinical availability, and low costs. Outcome variables were defined as overall survival and total recurrence (locoregional recurrence and distant recurrence). Cox regression was used to determine the prognostic factors, while binary logistic regression was used to calculate the probabilities of outcome variables up to the time points (e.g., 2-year, 3-year, 5-year, 8-year). The proportional hazard assumption was also checked. Clinical significance, expert opinion, and literature findings were prioritized over statistical findings in predictor selection, in accordance with methodological and analytical books. Furthermore, Pearson correlation analysis was employed to

ascertain the association between predictors. Examiners of outcome variables were blinded to relevant predictors. Also, predictor variable evaluators were blinded to both outcome variables and other predictors.

Kaplan–Meier analysis was also done for categorical predictors. A predictor's variance inflation factor (VIF) > 4, was deemed to indicate serious collinearity. In such cases, we combined the variables or eliminated the least clinically significant variable that was covered logically by other predictors. To minimize the information loss, we refrained from categorizing quantitative variables. Univariable hazard ratio (HR) analysis was performed. A comprehensive analysis using a multivariable model was also conducted. Since no "statistical" interaction effect was found in the existing literature and previous breast cancer models, we did not address it in our model. Diagnostic values, including area under the curve (AUC), along with goodness-of-fit measures such as Akaike information criterion (AIC), and Harrell's C, were utilized to evaluate the model's performance. Calibration analysis was performed for both Cox and binary logistic regressions using the Cox-Snell residual plot and bootstrap method, respectively.

The leave-one-out cross-validation was implemented to assess the model's internal validity instead of random/non-random splitting. To eliminate the possible overfitting, uniform shrinkage analysis was performed, and a calculator was developed to determine the probability of outcome occurrence. Time-dependent ROC curve was also plotted for Cox regression based on the hazard score. Besides, decision curve analysis was also done on shrunken coefficients to evaluate the clinical net benefit of using this prediction model. Our dataset had minimal missing values (< 4%), which were distributed across several variables. Multiple imputation method was used to account for the missing data, and complete case analysis was avoided. A p-value less than 0.05 was deemed to indicate statistical significance.

Results

Patient Characteristics

The study involved 922 consecutive breast cancer patients with a cumulative 3814 patient-year follow-ups. Of these patients, 62 (6.72%) died with a mean patient-year follow-up of 8.89 years (CI = 8.74 to 9.04), and 90 (9.76%) experienced any form of recurrence with mean patient-year follow-up of 8.20 years (CI = 7.92 to 8.48). The majority of these patients had invasive ductal carcinoma (IDC), which accounted for 89.0% of cases, while invasive lobular carcinoma (ILC) accounted for 9.8%. The remaining (3.2%) included other types of invasive breast cancers, such as metaplastic, mucinous, and tubular carcinomas. A summary of all predictors in relation to the survival and recurrence of the patients is provided in Table 1. Appendix D shows the overall Kaplan–Meier plots for survival and recurrence. Kaplan–Meier plots of survival rate based on each categorical predictor are presented in Appendix E. Also, the mean patient-day follow-up for each predictor is shown in Appendix F.

Predictor Selection Results

The correlogram in Appendix G shows the pairwise correlation coefficients between all predictors. The following predictors with VIF > 4 were identified as sources of collinearity: wash-in rate of breast tissue in T1-weighted pre- and post-contrast phases, the ratio of breast tissue being enhanced by more than 70% in T1-weighted pre-contrast phase, HER2 status, anti-HER2 therapy, and pathological response. To solve the issue, the wash-in rate of breast tissue in the T1-weighted pre-contrast phase and the ratio of breast tissue being enhanced by more than 70% in the T1-weighted pre-contrast phase were removed from the final model. Also, we merged the data of the radiological and pathological response of tumors and defined a new predictor as "tumor response" classified into three modes: no neoadjuvant therapy administered (reference layer), complete response, and incomplete response. We prioritized using pathological data in the controversy between radiological and pathological data. In addition, we combined the HER2 status and anti-HER2 therapy data and established a qualitative three-modal predictor: HER2 negative (reference layer), HER2 positive but not received anti-HER2 therapy, HER2 positive, and received anti-HER2 treatment. Finally, to enhance the consistency of our final model, we combined PR status and ER status. Then, we revised the hormone therapy predictor to a qualitative three-modal predictor: Both ER and PR receptor negative (reference layer), ER/PR receptor positive but not received hormone therapy, and ER/PR receptor positive and received hormone therapy. The collinearity parameters (e.g., VIF) before and after intervening are reported in Appendix H. Appendix I represents the univariable hazard ratios of the final predictors.

Full Model

The full model multivariable hazard ratios as well as bootstrapping and Jackknife method hazard ratios are shown in Table 2. Dominance analysis (see Appendix J for comprehensive analysis) identified the most predictive predictors as follows: (1) M status, (2) pectoral chest involvement, (3) tumor volume, and (4) wash-in rate. The survival model had an AIC value of 752.9, indicating a good fit of the model to the data. Similarly, the recurrence model had an AIC value of 1020.7. Lower AIC values generally suggest better model

Table 1 Characteristics of the included patients

		Survival			Total recurrence		
		Dead	Survival	*p*-value	Recurrence	No recurrence	*p*-value
Overall patient number		62 (6.7%)	860 (93.2%)		90 (9.7%)	832 (90.2%)	
HER2 status	Negative	54 (7.1%)	705 (92.8%)	0.187	74 (9.7%)	685 (90.2%)	0.953
	Positive and not received anti-HER2 therapy	3 (12.0%)	22 (88.0%)		3 (12%)	22 (88.0%)	
	Positive and received anti-HER2 therapy	5 (3.6%)	133 (96.3%)		13 (9.4%)	125 (90.5%)	
Chemotherapy	Not received	20 (5.9%)	318 (94.0%)	0.457	18 (5.3%)	320 (94.6%)	< 0.001
	Received	42 (7.1%)	542 (92.8%)		72 (12.3%)	512 (87.6%)	
Contralateral breast involvement	Absent	52 (6.7%)	718 (93.2%)	0.938	74 (9.6%)	696 (90.3%)	0.728
	Present	10 (6.5%)	142 (93.4%)		16 (10.5%)	136 (89.4%)	
Ethnicity	Other	4 (5.8%)	64 (94.1%)	0.025	7 (10.2%)	61 (89.7%)	0.061
	White	36 (5.5%)	615 (94.4%)		54 (8.2%)	597 (91.7%)	
	Black	22 (10.8%)	181 (89.1%)		29 (14.2%)	174 (85.7%)	
Hormonal therapy	Negative PR and ER	29 (13.0%)	194 (87.0%)	< 0.001	32 (14.3%)	191 (85.6%)	0.003
	Positive PR/ER and not received hormonal therapy	14 (13.0%)	93 (86.9%)		13 (12.1%)	94 (87.8%)	
	Positive PR/ER and received hormonal therapy	19 (3.2%)	573 (96.7%)		45 (7.6%)	547 (92.4%)	
Lymphovascular invasion	Absent	23 (3.6%)	604 (96.3%)	< 0.001	47 (7.5%)	580 (92.5%)	< 0.001
	Present	3.9 (13.2%)	256 (86.7%)		43 (14.5%)	252 (85.4%)	
M status	M0	51 (5.7%)	842 (94.2%)	< 0.001	87 (9.7%)	806 (90.2%)	0.914
	M1	11 (37.9%)	18 (62.0%)		3 (10.3%)	26 (89.6%)	
Menstrual status	Pre-menopause	23 (5.5%)	393 (94.4%)	0.189	42 (10.1%)	374 (89.9%)	0.756
	Post-menopause	39 (7.7%)	467 (92.2%)		48 (9.4%)	458 (90.5%)	
Multicentrality	Absent	34 (6.1%)	521 (93.8%)	0.373	45 (8.1%)	510 (91.8%)	0.038
	Present	28 (7.6%)	339 (92.3%)		45 (12.2%)	322 (87.7%)	
N status	N0	18 (3.4%)	511 (96.6%)	< 0.001	41 (7.7%)	488 (92.2%)	0.017
	N0 +	44 (11.2%)	349 (88.8%)		49 (12.4%)	344 (87.5%)	
Oophorectomy	Not performed	59 (7.1%)	763 (92.8%)	0.116	80 (9.7%)	742 (90.2%)	0.932
	Done	3 (3.0%)	97 (97.0%)		10 (10.0%)	90 (90.0%)	
Tumor response	Neoadjuvant therapy not received	40 (6.0%)	621 (93.9%)	0.046	54 (8.1%)	607 (91.8%)	< 0.001
	Complete response	1 (1.4%)	66 (98.5%)		1 (1.4%)	66 (98.5%)	
	Incomplete response	21 (10.8%)	173 (89.1%)		35 (18.0%)	159 (81.9%)	
Pectoral/chest involvement	Absent	54 (5.9%)	848 (94.0%)	< 0.001	85 (9.4%)	817 (90.5%)	0.020
	Present	8 (40.0%)	12 (60.0%)		5 (25.0%)	15 (75.0%)	
Radiotherapy	Not received	19 (6.8%)	259 (93.1%)	0.930	27 (9.7%)	251 (90.2%)	0.974
	Received	43 (6.6%)	601 (93.3%)		63 (9.7%)	581 (90.2%)	
Skin/nipple involvement	Absent	49 (5.8%)	789 (94.1%)	< 0.001	74 (8.8%)	764 (91.1%)	0.003
	Present	13 (15.4%)	71 (84.5%)		16 (19.0%)	68 (80.9%)	

Table 1 (continued)

		Survival			Total recurrence		
		Dead	Survival	*p*-value	Recurrence	No recurrence	*p*-value
Surgery type	Not performed	12 (27.9%)	31 (72.0%)	0.167	3 (6.9%)	40 (93.0%)	0.005
	Lumpectomy	19 (4.1%)	444 (95.9%)		33 (7.1%)	430 (92.8%)	
	Mastectomy	31 (7.4%)	385 (92.5%)		54 (12.9%)	362 (87.0%)	
T status	T1	17 (4.1%)	392 (95.8%)	< 0.001	26 (6.3%)	383 (93.6%)	< 0.001
	T2	26 (6.5%)	369 (93.4%)		43 (10.8%)	352 (89.1%)	
	T3	15 (16.6%)	75 (83.3%)		14 (15.5%)	76 (84.4%)	
	T4	4 (14.2%)	24 (85.7%)		7 (25.0%)	21 (75.0%)	
Surgery time	< 8 weeks	15 (3.3%)	435 (96.6%)	< 0.001	29 (6.4%)	421 (93.5%)	< 0.001
	> 8 weeks	47 (9.9%)	425 (90.0%)		61 (12.9%)	411 (87.0%)	
Size (cm)		6.2 (CI = 5.0 to 7.4)	3.6 (CI = 3.4 to 3.8)	< 0.001	5.6 (CI = 4.7 to 6.5)	3.6 (CI = 3.4 to 3.8)	< 0.001
Volume (cm^3)		31.6 (CI = 15.4 to 47.3)	8.3 (CI = 7.1 to 9.5)	< 0.001	22.1 (CI = 14.9 to 29.3)	8.5 (CI = 7.0 to 10.1)	< 0.001
Breast non-tumor volume (%)		30.8 (CI = 27.1 to 34.1)	28 (CI = 27.2 to 29.1)	0.155	29.5 (CI = 26.5 to 32.4)	28.2 (CI = 27.2 to 29.1)	0.411
Tumor SER in pre-contrast phase		0.963 (CI = 0.914 to 1.013)	0.930 (CI = 0.910 to 0.950)	0.389	0.973 (CI = 0.932 to 1.014)	0.928 (CI = 0.907 to 0.948)	0.169
Breast SER in pre-contrast phase		0.513 (CI = 0.489 to 0.536)	0.524 (CI = 0.518 to 0.530)	0.349	0.529 (CI = 0.512 to 0.545)	0.523 (CI = 0.516 to 0.529)	0.569
Breast SER in post-contrast phase		0.687 (CI = 0.654 to 0.720)	0.702 (CI = 0.692 to 0.711)	0.453	0.692 (CI = 0.668 to 0.716)	0.702 (CI = 0.691 to 0.712)	0.550
Tumor wash-in rate in pre-contrast phase		799 (CI = 579 to 1019)	627 (CI = 581 to 673)	0.062	677 (CI = 516 to 838)	634 (CI = 587 to 682)	0.584
Breast wash-in rate in pre-contrast phase		81.6 (CI = 63.9 to 99.4)	75.3 (CI = 70.5 to 80.1)	0.504	78.0 (CI = 62.8 to 93.1)	75.5 (CI = 70.7 to 80.4)	0.760
Time to peak (ms)		2.00 (CI = 1.74 to 2.26)	2.13 (CI = 2.07 to 2.20)	0.298	1.86 (CI = 1.66 to 2.06)	2.15 (CI = 2.09 to 2.22)	0.006
Age (year)		54.3 (CI = 51.3 to 57.2)	52.8 (CI = 52.1 to 53.6)	0.338	51.1 (CI = 48.6 to 53.6)	53.1 (CI = 52.4 to 53.9)	0.103
Nottingham score		7.32 (CI = 6.9 7.6 to)	6.7 (CI = 6.6 to 6.8)	0.002	7.4 (CI = 7.1 to 7.7)	6.6 (CI = 6.5 to 6.7)	< 0.001

fit relative to the number of parameters included. Harrell's C-statistic was 0.84 for the survival model and 0.81 for the recurrence model. Also, the goodness of fit plot (i.e., calibration plot) for the survival prediction model is represented in Appendix K. The proportional hazard assumption was normal (p-value = 0.330). Full model AUCs in 8-, 5-, 3-, and 2-year survivals were 0.834 (CI = 0.809 to 0.858), 0.838 (CI = 0.812 to 0.861), 0.876 (CI = 0.853 to 0.897), and 0.891 (CI = 0.869 to 0.910), respectively. Also, full model AUCs in 8-, 5-, and 3-year recurrences were 0.776 (CI = 0.748 to 0.803), 0.808 (CI = 0.780 to 0.834), and 0.892 (CI = 0.869 to 0.913), respectively. Figure 2 displays the time-dependent receiver operating characteristic (ROC) curves for both survival and recurrence full models. The sensitivity and specificity of the survival model based on Youden optimal cut point of hazard score > 2.38 were 80.8% and 69.2% with a good AUC of 0.813. Also, the sensitivity and specificity of the recurrence model based on Youden optimal cut point of hazard score > 4.46 were 73.7% and 79.0% with a good AUC of 0.790. Finally, Appendix L depicts the full model multivariable odds ratios for 8-, 5-, 3-, and 2-year survivals and 8-, 5-, and 3-year recurrences.

Internal Validation Using Leave-one-out Method

Figure 3 shows ROC curves comparing development and validation models in 8-, 5-, 3-, and 2-year survivals. Adjusted AUCs were 0.740 (CI = 0.711 to 0.768), 0.741 (CI = 0.712 to 0.770), 0.788 (CI = 0.761 to 0.816), and 0.783 (CI = 0.755 to 0.809), respectively. Also, ROC curves for the full model in 8-, 5-, and 3-year recurrences are represented in Appendix M. Adjusted AUCs were 0.678 (CI = 0.647 to

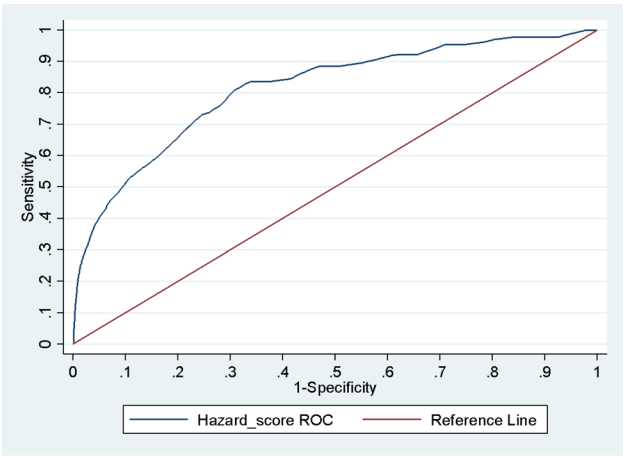
Table 2 Full model multivariable hazard ratios

		Hazard ratio (survival)	Hazard ratio (recurrence)	Bootstrap hazard ratio (survival)	Bootstrap hazard ratio (recurrence)	Jackknife hazard ratio (survival)	Jackknife hazard ratio (recurrence)
HER2 status	Positive HER2 and not received hormonal therapy	0.29 (CI = 0.06 to 1.46)	0.78 (CI = 0.17 to 3.62)	N/A	N/A	0.29 (CI = 0.02 to 3.91)	0.78 (CI = 0.07 to 9.19)
	Positive HER2 and received hormonal therapy	0.39 (CI = 0.15 to 1.03)	0.57 (CI = 0.30 to 1.09)	N/A	0.57 (CI = 0.26 to 1.25)	0.39 (CI = 0.12 to 1.30)	0.57 (CI = 0.26 to 1.25)
Chemotherapy		0.78 (CI = 0.31 to 1.99)	0.91 (CI = 0.44 to 1.87)	0.78 (CI = 0.22 to 2.76)	0.91 (CI = 0.37 to 2.25)	0.78 (CI = 0.25 to 2.46)	0.91 (CI = 0.38 to 2.20)
Contralateral breast involvement		1.13 (CI = 0.54 to 2.36)	1.07 (CI = 0.58 to 1.96)	1.13 (CI = 0.42 to 3.07)	1.07 (CI = 0.48 to 2.40)	1.13 (CI = 0.49 to 2.64)	1.07 (CI = 0.48 to 2.36)
Ethnicity	White	0.99 (CI = 0.32 to 3.00)	0.80 (CI = 0.35 to 1.82)	0.99 (CI = 0.00 to 203.31)	0.80 (CI = 0.15 to 4.19)	0.99 (CI = 0.19 to 5.06)	0.80 (CI = 0.30 to 2.13)
	Black	0.87 (CI = 0.26 to 2.94)	0.60 (CI = 0.24 to 1.49)	0.87 (CI = 0.00 to 186.42)	0.60 (CI = 0.10 to 3.55)	0.87 (CI = 0.15 to 5.19)	0.60 (CI = 0.19 to 1.91)
Hormonal therapy	Positive PR/ER and not received hormonal therapy	0.72 (CI = 0.28 to 1.88)	2.06 (CI = 0.96 to 4.45)	0.72 (CI = 0.19 to 2.71)	2.06 (CI = 0.79 to 5.38)	0.72 (CI = 0.19 to 2.68)	2.06 (CI = 0.83 to 5.12)
	Positive PR/ER and received hormonal therapy	0.21 (CI = 0.10 to 0.43)	0.48 (CI = 0.28 to 0.84)	0.21 (CI = 0.08 to 0.54)	0.48 (CI = 0.25 to 0.95)	0.21 (CI = 0.09 to 0.50)	0.48 (CI = 0.24 to 0.97)
Lymphovascular invasion		2.26 (CI = 1.11 to 4.58)	1.89 (CI = 1.08 to 3.29)	2.26 (CI = 0.96 to 5.34)	1.89 (CI = 0.97 to 3.68)	2.26 (CI = 0.98 to 5.21)	1.89 (CI = 0.95 to 3.77)
M status		1.02 (CI = 0.22 to 4.68)	0.18 (CI = 0.03 to 1.10)	1.02 (CI = 0.10 to 10.40)	N/A	1.02 (CI = 0.10 to 10.07)	0.18 (CI = 0.01 to 3.53)
Menstrual status		1.11 (CI = 0.51 to 2.41)	1.26 (CI = 0.66 to 2.39)	1.11 (CI = 0.46 to 2.66)	1.26 (CI = 0.58 to 2.75)	1.11 (CI = 0.50 to 2.47)	1.26 (CI = 0.61 to 2.60)
Multicentrality		0.81 (CI = 0.45 to 1.46)	1.32 (CI = 0.81 to 2.13)	0.81 (CI = 0.35 to 1.89)	1.32 (CI = 0.71 to 2.45)	0.81 (CI = 0.35 to 1.88)	1.32 (CI = 0.70 to 2.48)
N status		1.67 (CI = 0.80 to 3.49)	1.12 (CI = 0.64 to 1.95)	1.67 (CI = 0.59 to 4.77)	1.12 (CI = 0.55 to 2.27)	1.67 (CI = 0.65 to 4.33)	1.12 (CI = 0.55 to 2.28)
Oophorectomy		0.54 (CI = 0.15 to 1.93)	0.76 (CI = 0.37 to 1.59)	N/A	0.76 (CI = 0.32 to 1.84)	0.54 (CI = 0.12 to 2.48)	0.76 (CI = 0.35 to 1.68)
Tumor response	Complete response	0.09 (CI = 0.01 to 0.77)	0.04 (CI = 0.01 to 0.32)	N/A	N/A	N/A	N/A
	Incomplete response	0.93 (CI = 0.41 to 2.10)	0.81 (CI = 0.43 to 1.53)	0.93 (CI = 0.35 to 2.46)	0.81 (CI = 0.37 to 1.80)	0.93 (CI = 0.35 to 2.45)	0.81 (CI = 0.36 to 1.84)
Pectoral/chest involvement		3.55 (CI = 1.21 to 10.40)	3.32 (CI = 1.12 to 9.84)	3.55 (CI = 0.85 to 14.80)	N/A	3.55 (CI = 0.89 to 14.19)	3.32 (CI = 0.65 to 16.93)

Table 2 (continued)

		Hazard ratio (survival)	Hazard ratio (recurrence)	Bootstrap hazard ratio (survival)	Bootstrap hazard ratio (recurrence)	Jackknife hazard ratio (survival)	Jackknife hazard ratio (recurrence)
Radiotherapy		1.02 (CI = 0.49 to 2.15)	0.76 (CI = 0.42 to 1.37)	1.02 (CI = 0.38 to 2.77)	0.76 (CI = 0.37 to 1.58)	1.02 (CI = 0.40 to 2.63)	0.76 (CI = 0.36 to 1.61)
Skin/nipple involvement		1.01 (CI = 0.44 to 2.32)	0.99 (CI = 0.46 to 2.16)	1.01 (CI = 0.33 to 3.13)	0.99 (CI = 0.37 to 2.69)	1.01 (CI = 0.34 to 2.96)	0.99 (CI = 0.37 to 2.66)
Surgery type	Lumpectomy	0.78 (CI = 0.18 to 3.39)	2.13 (CI = 0.35 to 12.80)	0.78 (CI = 0.10 to 6.14)	N/A	0.78 (CI = 0.09 to 6.51)	2.13 (CI = 0.07 to 60.87)
	Mastectomy	1.07 (CI = 0.29 to 3.90)	2.48 (CI = 0.46 to 13.33)	1.07 (CI = 0.14 to 8.14)	N/A	1.07 (CI = 0.13 to 9.15)	2.48 (CI = 0.09 to 68.85)
T status	T2	1.26 (CI = 0.64 to 2.50)	1.46 (CI = 0.85 to 2.50)	1.26 (CI = 0.50 to 3.21)	1.46 (CI = 0.70 to 3.07)	1.26 (CI = 0.53 to 3.02)	1.46 (CI = 0.74 to 2.87)
	T3	1.59 (CI = 0.67 to 3.78)	1.73 (CI = 0.78 to 3.86)	1.59 (CI = 0.49 to 5.20)	1.73 (CI = 0.59 to 5.10)	1.59 (CI = 0.52 to 4.87)	1.73 (CI = 0.63 to 4.78)
	T4	1.22 (CI = 0.30 to 5)	3.68 (CI = 1.25 to 10.87)	N/A	3.68 (CI = 0.15 to 87.43)	1.22 (CI = 0.21 to 7.08)	3.68 (CI = 1.03 to 13.18)
Surgery time		1.79 (CI = 0.78 to 4.10)	1.87 (CI = 1.02 to 3.43)	1.79 (CI = 0.68 to 4.70)	1.87 (CI = 0.86 to 4.05)	1.79 (CI = 0.73 to 4.38)	1.87 (CI = 0.88 to 3.97)
Size (cm)		1.18 (CI = 1.08 to 1.30)	1.15 (CI = 1.05 to 1.25)	1.18 (CI = 1.01 to 1.39)	1.15 (CI = 1.01 to 1.31)	1.18 (CI = 1 to 1.40)	1.15 (CI = 1.00 to 1.32)
Volume (cm^3)		0.99 (CI = 0.99 to 1.00)	1.00 (CI = 0.99 to 1.00)	0.99 (CI = 0.97 to 1.01)	1.00 (CI = 0.98 to 1.02)	0.99 (CI = 0.96 to 1.02)	1.00 (CI = 0.97 to 1.02)
Breast non-tumor volume (%)		1.02 (CI = 1 to 1.04)	1.00 (CI = 0.98 to 1.02)	1.02 (CI = 0.99 to 1.05)	1.00 (CI = 0.98 to 1.02)	1.02 (CI = 0.99 to 1.04)	1.00 (CI = 0.98 to 1.03)
Tumor SER in pre-contrast phase		0.79 (CI = 0.24 to 2.60)	0.83 (CI = 0.30 to 2.25)	0.79 (CI = 0.26 to 2.39)	0.83 (CI = 0.32 to 2.11)	0.79 (CI = 0.29 to 2.18)	0.83 (CI = 0.33 to 2.06)
Breast SER in pre-contrast phase		0.07 (CI = 0.00 to 8.52)	3.24 (CI = 0.04 to 278.99)	0.07 (CI = 0.00 to 38.49)	N/A	0.07 (CI = 0.00 to 25.57)	N/A
Breast SER in post-contrast phase		1.75 (CI = 0.09 to 35.02)	0.47 (CI = 0.03 to 7.05)	1.75 (CI = 0.04 to 68.52)	0.47 (CI = 0.01 to 15.76)	1.75 (CI = 0.05 to 65.12)	0.47 (CI = 0.01 to 15.79)
Tumor wash-in rate in pre-contrast phase		1.00 (CI = 1.00 to 1.00)	1.00 (CI = 1.00 to 1.00)	1.00 (CI = 1.00 to 1.00)	1.00 (CI = 1.00 to 1.00)	1.00 (CI = 1.00 to 1.00)	1.00 (CI = 1.00 to 1.00)
Breast wash-in rate in pre-contrast phase		1.00 (CI = 0.99 to 1.00)	1.00 (CI = 0.99 to 1.00)	1.00 (CI = 0.99 to 1.01)	1.00 (CI = 0.99 to 1.00)	1.00 (CI = 0.99 to 1.00)	1.00 (CI = 0.99 to 1.00)
Time to peak (ms)		0.97 (CI = 0.70 to 1.35)	0.73 (CI = 0.56 to 0.95)	0.97 (CI = 0.62 to 1.52)	0.73 (CI = 0.52 to 1.01)	0.97 (CI = 0.66 to 1.44)	0.73 (CI = 0.53 to 1.00)
Age (year)		1.02 (CI = 0.98 to 1.06)	0.99 (CI = 0.96 to 1.02)	1.02 (CI = 0.98 to 1.06)	0.99 (CI = 0.95 to 1.02)	1.02 (CI = 0.98 to 1.06)	0.99 (CI = 0.95 to 1.02)
Nottingham score		1.07 (CI = 0.84 to 1.35)	1.28 (CI = 1.06 to 1.54)	1.07 (CI = 0.81 to 1.41)	1.28 (CI = 1.02 to 1.61)	1.07 (CI = 0.82 to 1.39)	1.28 (CI = 1.03 to 1.59)

A:



B:

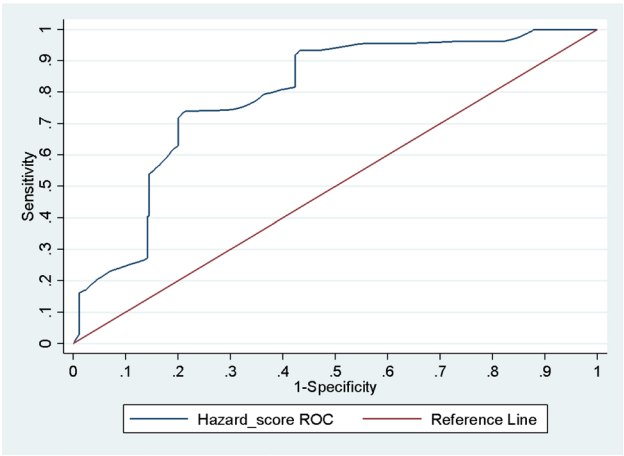


Fig. 2 **A** Time-dependent receiver operating characteristic (ROC) curve for survival full model. **B** Time-dependent ROC curve for recurrence

0.708), 0.696 (CI = 0.664 to 0.727), and 0.769 (CI = 0.740 to 0.798), respectively.

Shrinkage Analysis and Decision Curve Analysis

Shrinkage analysis findings are presented in Tables 3 and 4 for survival and recurrence, respectively. Bootstrap shrinkage values for 8-, 5-, 3-, and 2-year survival models were 0.685, 0.686, 0.641, and 0.580, and adjusted AUCs slightly diminishing to 0.758 (CI = 0.700 to 0.811), 0.762 (CI = 0.703 to 0.816), 0.808 (CI = 0.746 to 0.860), and 0.814 (CI = 0.733 to 0.878). Also, bootstrap shrinkage values for 8-, 5-, and 3-year recurrences were 0.648, 0.637, and 0.585, and adjusted AUCs were 0.697 (CI = 0.644 to 0.742), 0.727 (CI = 0.672 to 0.780), and 0.818 (CI = 0.742 to 0.874), in that order. All AUCs for full, leave-one-out, and shrinkage models are represented in Table 5.

Figure 4 illustrates decision analysis curves that point to a positive net benefit in using this model throughout the range of 0 to 40% probability of death and recurrence based on shrunken values. Also, the calibration plots and their parameters are represented in Appendix N. Regarding these issues, the model provides excellent calibration and clinical utility for the shrinkage models.

Introducing a User-friendly Calculator

For clinical applicability purposes, all detailed statistical reports mentioned above were implemented in the calculator's background for ease of use to determine each patient's personalized hazard scores and probabilities of death and recurrence up to different time points. The calculator file is available in Appendix O. In addition, three real-patient examples are shown in Appendix P for further clinical elaboration and explanation: (1) a 41-year-old patient that survived without recurrence (5-year survival probability of 4.4% and 5-year recurrence probability of 8.5% based on calculator); (2) a 47-year-old female survived but had recurrence in 5- and 8-year periods from diagnosis (5-year survival probability of 2.4% and 5-year recurrence probability of 7.2% based on calculator); (3) a 54-year-old-patient that passed away and had developed recurrence as well (5-year survival probability of 20.0% and 5-year recurrence probability of 33.4% based on calculator).

Discussion

DCE-MRI enables the non-invasive and in vivo evaluation of the vascular dynamics of tumors, which can be utilized to objectively evaluate the development of neovascularization and quantify their perfusion, tissue non-tumor volume, tumor dimensions, invasion, and various other parameters. These countless qualitative and quantitative MRI findings have been demonstrated to be associated with other conventional prognostic markers [15–18]. Based on these relationships between radiologic findings and breast cancer prognosis, we developed and internally validated prognostic prediction models based on DCE-MRI, pathological, and clinical findings in several time-points in our present investigation. The AUC values for our internally validated models demonstrated robust performance, ranging between 0.740 and 0.783 for 8-year, 5-year, 3-year, and 2-year survival predictions. Also, internally validated models AUC in 8-, 5-, and 3-year recurrences ranged between 0.678 and 0.769, indicating the good predictive performance of our models.

This study employed a multidisciplinary approach, incorporating expertise from oncology, gynecology, pathology, radiology, and surgery. This collaborative approach enhances the generalizability of the findings to real-world

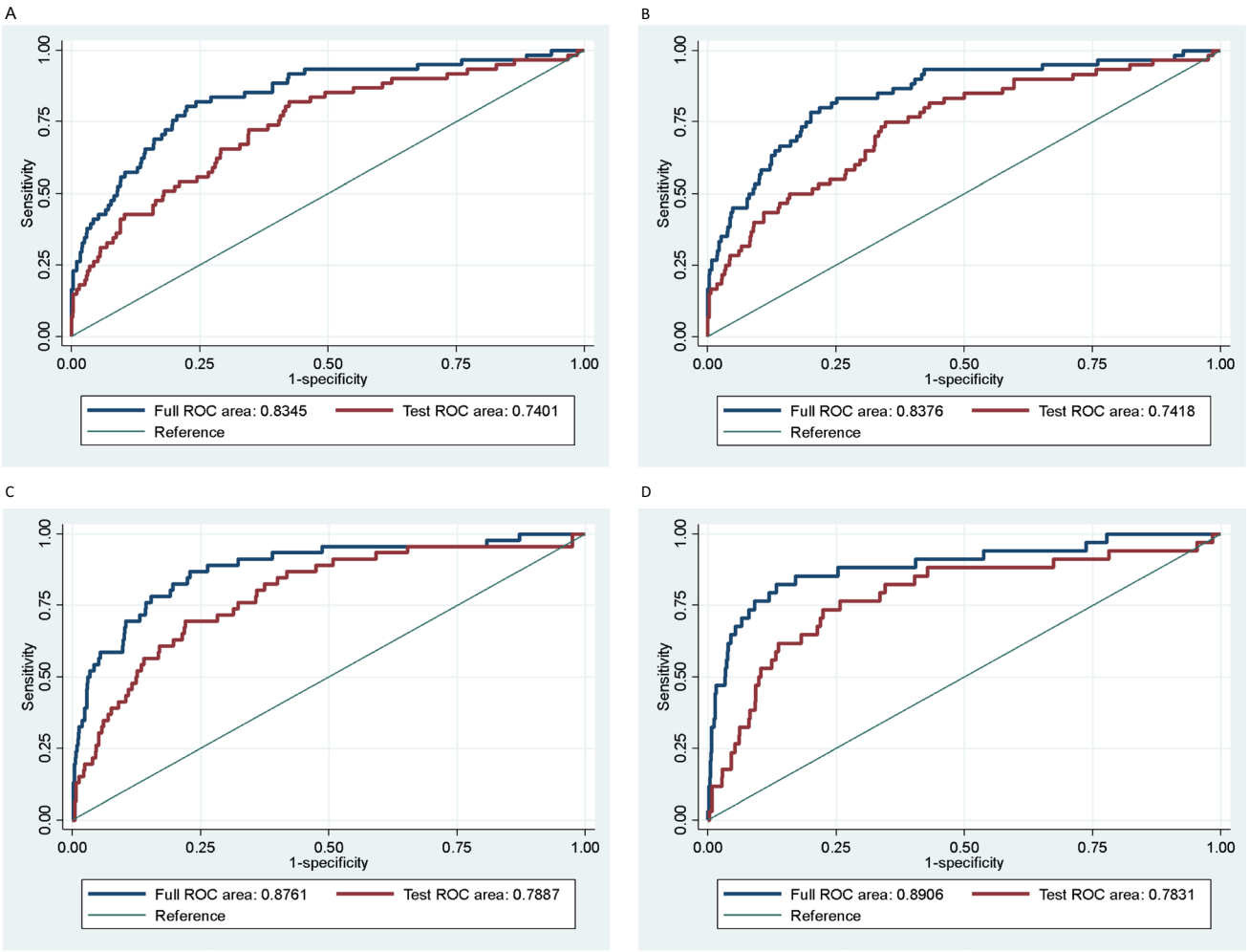


Fig. 3 **A** Receiver operating characteristic (ROC) curve for full and test models in an 8-year survival. **B** ROC curve for full and test models in a 5-year survival. **C** ROC curve for full and test models in a 3-year survival. **D** ROC curve for full model and test model in a 2-year survival

clinical settings. The aim of this study was to establish the relationship between clinical, pathological, and radiologic factors and their ability to predict patient survival and recurrence, which is critical for personalized treatment plans and selecting appropriate surgical interventions and therapeutic regimens. The PREDICT model, a well-established breast cancer prognostic tool, incorporates variables such as age, tumor size, grade, lymph node status, estrogen receptor status, HER2 status, and whether chemotherapy or hormone therapy was received. While PREDICT provides robust predictions based on traditional clinical factors, it does not include imaging parameters [19]. Adjuvant! Online also employs clinical and pathological factors to predict neoadjuvant therapy indications, recurrence, and survival probabilities [20]. It includes tumor size, grade, estrogen receptor status, and lymph node status. Similar to PREDICT, Adjuvant! Online does not incorporate imaging data, which our model integrates to enhance predictive accuracy. We employed a broad inclusion criterion and a large sample size in order to avoid limitations associated with focusing on specific breast cancer subsets (e.g., triple-negative, DCIS, T2 N0M0, or unilateral) and ensures the results apply to a broader range of patients encountered in clinical settings. Another key strength of our study lies in the extensive follow-up period. The risk of breast cancer recurrence is highest within 3 years after diagnosis since 70% of early recurrences occur within this timeframe. Additionally, individuals who experience early recurrence tend to have a shorter median survival, and a more intense and aggressive disease course [21]. After that, the risk decreases quickly, and patients who have been disease-free for 8 years are unlikely to die from breast cancer [22]. Unlike many studies focusing solely on 5-year or less survival, our data allowed us to analyze survival and recurrence rates at various time points, including 2, 3, 5, and 8 years. This comprehensive picture provides valuable insights into patient outcomes over a longer timeframe. It

Table 3 Odds ratios and coefficients based on bootstrap shrinkage method for 8, 5, 3, and 2-year survival models

		8-year survival shrinkage analysis		5-year survival shrinkage analysis		3-year survival shrinkage analysis		2-year survival shrinkage analysis	
		Odds ratio	Coefficient	Odds ratio	Coefficient	Odds ratio	Coefficient	Odds ratio	Coefficient
HER2 status	Positive HER2 and not received hormonal therapy	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	Positive HER2 and received hormonal therapy	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Chemotherapy		1.17 (CI = 0.60 to 2.25)	0.15 (CI = − 0.50 to 0.81)	1.10 (CI = 0.56 to 2.13)	0.09 (CI = − 0.57 to 0.76)	1.07 (CI = 0.50 to 2.29)	0.07 (CI = − 0.69 to 0.83)	0.58 (CI = 0.16 to 2.11)	0.10 (CI = − 0.68 to 0.88)
Contralateral breast involvement		1.08 (CI = 0.62 to 1.87)	0.07 (CI = − 0.48 to 0.63)	1.11 (CI = 0.63 to 1.94)	0.10 (CI = − 0.45 to 0.66)	1.10 (CI = 0.60 to 2.00)	0.09 (CI = − 0.51 to 0.69)	0.89 (CI = 0.46 to 1.73)	− 0.11 (CI = − 0.78 to 0.55)
Ethnicity	White	1.09 (CI = 0.46 to 2.56)	0.08 (CI = − 0.77 to 0.94)	1.05 (CI = 0.45 to 2.49)	0.05 (CI = − 0.81 to 0.91)	1.68 (CI = 0.58 to 4.83)	0.52 (CI = − 0.54 to 1.58)	1.27 (CI = 0.48 to 3.38)	0.24 (CI = − 0.74 to 1.22)
	Black	1.12 (CI = 0.45 to 2.77)	0.11 (CI = − 0.79 to 1.02)	1.11 (CI = 0.45 to 2.74)	0.10 (CI = − 0.80 to 1.01)	1.71 (CI = 0.57 to 5.15)	0.54 (CI = − 0.57 to 1.64)	1.46 (CI = 0.53 to 4.06)	0.38 (CI = − 0.64 to 1.40)
Hormonal therapy	Positive PR/ER and not received hormonal therapy	0.88 (CI = 0.46 to 1.70)	− 0.12 (CI =—− 0.78 to 0.53)	0.78 (CI = 0.40 to 1.54)	− 0.25 (CI = − 0.93 to 0.43)	0.68 (CI = 0.33 to 1.38)	− 0.39 (CI = − 1.09 to 0.32)	0.75 (CI = 0.36 to 1.54)	− 0.29 (CI = − 1.01 to 0.43)
	Positive PR/ER and received hormonal therapy	0.46 (CI = 0.28 to 0.77)	− 0.77 (CI = − 1.28 to − 0.26)	0.46 (CI = 0.28 to 0.77)	− 0.77 (CI = − 1.29 to − 0.26)	0.32 (CI = 0.18 to 0.56)	− 1.14 (CI = − 1.71 to − 0.57)	0.33 (CI = 0.18 to 0.60)	− 1.10 (CI = − 1.70 to − 0.50)
Lymphovascular invasion		1.58 (CI = 0.95 to 2.63)	0.46 (CI = − 0.06 to 0.97)	1.66 (CI = 0.99 to 2.80)	0.51 (CI = − 0.01 to 1.03)	2.45 (CI = 1.37 to 4.37)	0.89 (CI = 0.31 to 1.47)	2.92 (CI = 1.53 to 5.57)	1.07 (CI = 0.43 to 1.72)
M status		2.34 (CI = 0.88 to 6.25)	0.85 (CI = − 0.13 to 1.83)	2.53 (CI = 0.93 to 6.87)	0.93 (CI = − 0.07 to 1.93)	1.97 (CI = 0.69 to 5.62)	0.68 (CI = − 0.37 to 1.73)	1.67 (CI = 0.59 to 4.78)	0.51 (CI = − 0.53 to 1.56)
Menstrual status		1.07 (CI = 0.58 to 2.00)	0.07 (CI = − 0.55 to 0.69)	1.08 (CI = 0.58 to 2.04)	0.08 (CI = − 0.55 to 0.71)	1.22 (CI = 0.62 to 2.39)	0.20 (CI = − 0.48 to 0.87)	1.25 (CI = 0.61 to 2.54)	0.22 (CI = − 0.49 to 0.93)
Multicentrality		0.87 (CI = 0.56 to 1.37)	− 0.13 (CI = − 0.59 to 0.32)	0.91 (CI = 0.58 to 1.44)	− 0.09 (CI = − 0.55 to 0.37)	0.89 (CI = 0.55 to 1.44)	− 0.11 (CI = − 0.59 to 0.36)	0.92 (CI = 0.56 to 1.50)	− 0.09 (CI = − 0.58 to 0.41)
N status		1.37 (CI = 0.81 to 2.31)	0.31 (CI = − 0.21 to 0.84)	1.29 (CI = 0.75 to 2.19)	0.25 (CI = − 0.28 to 0.79)	1.31 (CI = 0.74 to 2.34)	0.27 (CI = − 0.30 to 0.85)	1.20 (CI = 0.66 to 2.19)	0.18 (CI = − 0.42 to 0.78)
Oophorectomy		0.68 (CI = 0.27 to 1.70)	− 0.38 (CI = − 1.30 to 0.53)	0.69 (CI = 0.28 to 1.73)	− 0.37 (CI = − 1.29 to 0.55)	0.65 (CI = 0.23 to 1.81)	− 0.43 (CI = − 1.47 to 0.60)	0.65 (CI = 0.23 to 1.81)	− 0.54 (CI = − 1.82 to 0.75)

Table 3 (continued)

		8-year survival shrinkage analysis		5-year survival shrinkage analysis		3-year survival shrinkage analysis		2-year survival shrinkage analysis	
		Odds ratio	Coefficient	Odds ratio	Coefficient	Odds ratio	Coefficient	Odds ratio	Coefficient
Tumor response	Complete response	0.19 (CI = 0.04 to 0.87)	− 1.68 (CI = − 3.24 to − 0.13)	0.19 (CI = 0.04 to 0.91)	− 1.66 (CI = − 3.23 to − 0.09)	0.24 (CI = 0.06 to 1.05)	− 1.41 (CI = − 2.86 to 0.04)	0.34 (CI = 0.09 to 1.32)	− 1.09 (CI = − 2.46 to 0.28)
	Incomplete response	1.04 (CI = 0.57 to 1.89)	0.04 (CI = − 0.56 to 0.64)	1.10 (CI = 0.60 to 2.03)	0.10 (CI = − 0.52 to 0.71)	1.15 (CI = 0.59 to 2.22)	0.14 (CI = − 0.52 to 0.80)	1.08 (CI = 0.54 to 2.15)	0.07 (CI = − 0.62 to 0.77)
Pectoral/chest involvement		3.27 (CI = 1.36 to 7.89)	1.18 (CI = 0.30 to 2.07)	3.27 (CI = 1.35 to 7.93)	1.18 (CI = 0.30 to 2.07)	2.52 (CI = 1.05 to 6.05)	0.93 (CI = 0.05 to 1.80)	2.31 (CI = 0.99 to 5.41)	0.84 (CI = − 0.01 to 1.69)
Radiotherapy		1.01 (CI = 0.60 to 1.71)	0.01 (CI = − 0.52 to 0.53)	1.05 (CI = 0.61 to 1.80)	0.05 (CI = − 0.49 to 0.59)	0.91 (CI = 0.52 to 1.59)	− 0.09 (CI = − 0.65 to 0.47)	0.87 (CI = 0.49 to 1.53)	− 0.14 (CI = − 0.71 to 0.43)
Skin/nipple involvement		0.95 (CI = 0.50 to 1.83)	− 0.05 (CI = − 0.70 to 0.61)	0.96 (CI = 0.50 to 1.86)	− 0.04 (CI = − 0.70 to 0.62)	1.34 (CI = 0.70 to 2.53)	0.29 (CI = − 0.35 to 0.93)	1.31 (CI = 0.69 to 2.50)	0.27 (CI = − 0.37 to 0.91)
Surgery type	Lumpectomy	1.22 (CI = 0.47 to 3.22)	0.20 (CI = − 0.76 to 1.17)	1.20 (CI = 0.44 to 3.20)	0.18 (CI = − 0.81 to 1.16)	1.27 (CI = 0.45 to 3.55)	0.24 (CI = − 0.80 to 1.27)	1.32 (CI = 0.46 to 3.76)	0.27 (CI = − 0.78 to 1.33)
	Mastectomy	1.34 (CI = 0.56 to 3.19)	0.29 (CI = − 0.58 to 1.16)	1.26 (CI = 0.52 to 3.06)	0.23 (CI = − 0.65 to 1.12)	1.44 (CI = 0.59 to 3.55)	0.37 (CI = − 0.53 to 1.27)	1.44 (CI = 0.58 to 3.56)	0.36 (CI = − 0.55 to 1.27)
T status	T2	0.99 (CI = 0.60 to 1.64)	− 0.01 (CI = − 0.51 to 0.49)	0.96 (CI = 0.58 to 1.59)	− 0.04 (CI = − 0.55 to 0.46)	0.98 (CI = 0.57 to 1.68)	− 0.02 (CI = − 0.55 to 0.52)	0.95 (CI = 0.54 to 1.67)	− 0.05 (CI = − 0.61 to 0.51)
	T3	1.31 (CI = 0.67 to 2.55)	0.27 (CI = − 0.40 to 0.93)	1.30 (CI = 0.67 to 2.56)	0.26 (CI = − 0.41 to 0.94)	1.27 (CI = 0.63 to 2.57)	0.24 (CI = − 0.47 to 0.94)	1.13 (CI = 0.55 to 2.35)	0.12 (CI = − 0.61 to 0.85)
	T4	0.64 (CI = 0.20 to 2.01)	− 0.45 (CI = − 1.60 to 0.70)	0.66 (CI = 0.21 to 2.07)	− 0.42 (CI = − 1.57 to 0.73)	0.58 (CI = 0.18 to 1.85)	− 0.55 (CI = − 1.71 to 0.62)	0.69 (CI = 0.23 to 2.07)	− 0.37 (CI = − 1.47 to 0.73)
Surgery time		1.41 (CI = 0.78 to 2.55)	0.34 (CI = − 0.25 to 0.93)	1.31 (CI = 0.71 to 2.40)	0.27 (CI = − 0.34 to 0.88)	1.31 (CI = 0.58 to 2.20)	0.13 (CI = − 0.54 to 0.79)	1.01 (CI = 0.51 to 2.02)	0.01 (CI = − 0.68 to 0.70)
Size (cm)		1.08 (CI = 0.99 to 1.17)	0.08 (CI = − 0.01 to 0.16)	1.08 (CI = 0.99 to 1.17)	0.08 (CI = − 0.01 to 0.16)	1.10 (CI = 1.02 to 1.19)	0.10 (CI = 0.02 to 0.18)	1.13 (CI = 1.04 to 1.22)	0.12 (CI = 0.04 to 0.20)
Volume (cm3)		1.00 (CI = 0.99 to 1.01)	0.00 (CI = − 0.01 to 0.01)	1.00 (CI = 0.99 to 1.01)	0.00 (CI = − 0.01 to 0.01)	0.99 (CI = 0.99 to 1.00)	− 0.01 (CI = − 0.01 to 0.00)	0.99 (CI = 0.99 to 1.00)	− 0.01 (CI = − 0.01 to 0.00)
Breast non-tumor volume (%)		1.01 (CI = 0.99 to 1.03)	0.01 (CI = − 0.01 to 0.03)	1.01 (CI = 0.99 to 1.03)	0.01 (CI = − 0.01 to 0.02)	1.00 (CI = 0.99 to 1.03)	0.01 (CI = − 0.01 to 0.03)	1.01 (CI = 1.00 to 1.03)	0.01 (CI = 0.00 to 0.03)
Tumor SER in pre-contrast phase		0.86 (CI = 0.36 to 2.10)	− 0.15 (CI = − 1.04 to 0.74)	0.93 (CI = 0.37 to 2.32)	− 0.07 (CI = − 0.98 to 0.84)	0.90 (CI = 0.33 to 2.44)	− 0.11 (CI = − 1.11 to 0.89)	0.79 (CI = 0.28 to 2.29)	− 0.23 (CI = − 1.29 to 0.83)
Breast SER in pre-contrast phase		0.12 (CI = 0.00 to 3.66)	− 2.16 (CI = − 5.61 to 1.30)	0.06 (CI = 0.00 to 2.05)	− 2.74 (CI = − 6.20 to 0.72)	0.06 (CI = 0.00 to 2.76)	− 2.85 (CI = − 6.71 to 1.01)	0.06 (CI = 0.00 to 3.92)	− 2.78 (CI = − 6.93 to 1.37)
Breast SER in post-contrast phase		2.02 (CI = 0.22 to 18.96)	0.70 (CI = − 1.54 to 2.94)	2.19 (CI = 0.23 to 20.75)	0.79 (CI = − 1.46 to 3.03)	2.19 (CI = 0.20 to 28.50)	0.87 (CI = − 1.60 to 3.35)	1.84 (CI = 0.13 to 26.30)	0.61 (CI = − 2.05 to 3.27)

Table 3 (continued)

	8-year survival shrinkage analysis		5-year survival shrinkage analysis		3-year survival shrinkage analysis		2-year survival shrinkage analysis	
	Odds ratio	Coefficient	Odds ratio	Coefficient	Odds ratio	Coefficient	Odds ratio	Coefficient
Tumor wash-in rate in pre-contrast phase	1.00 (CI = 1.00 to 1.00)	0.00 (CI = 0.00 to 0.00)	1.00 (CI = 1.00 to 1.00)	0.00 (CI = 0.00 to 0.00)	1.00 (CI = 1.00 to 1.00)	0.00 (CI = 0.00 to 0.00)	1.00 (CI = 1.00 to 1.00)	0.00 (CI = 0.00 to 0.00)
Breast wash-in rate in pre-contrast phase	1.00 (CI = 1.00 to 1.00)	0.00 (CI = 0.00 to 0.00)	1.00 (CI = 1.00 to 1.00)	0.00 (CI = 0.00 to 0.00)	1.00 (CI = 0.99 to 1.00)	0.00 (CI = − 0.01 to 0.00)	1.00 (CI = 1.00 to 1.01)	0.00 (CI = 0.00 to 0.01)
Time to peak (ms)	1.03 (CI = 0.81 to 1.31)	0.03 (CI = − 0.21 to 0.27)	1.03 (CI = 0.80 to 1.31)	0.03 (CI = − 0.22 to 0.27)	0.97 (CI = 0.74 to 1.27)	− 0.03 (CI = − 0.30 to 0.24)	0.87 (CI = 0.66 to 1.16)	− 0.14 (CI = − 0.42 to 0.15)
Age (year)	1.02 (CI = 0.99 to 1.05)	0.02 (CI = − 0.01 to 0.05)	1.02 (CI = 0.99 to 1.05)	0.02 (CI = − 0.01 to 0.05)	1.01 (CI = 0.98 to 1.04)	0.01 (CI = − 0.02 to 0.04)	1.02 (CI = 0.99 to 1.05)	0.02 (CI = − 0.01 to 0.05)
Nottingham score	1.04 (CI = 0.87 to 1.24)	0.04 (CI = − 0.13 to 0.21)	1.05 (CI = 0.88 to 1.25)	0.05 (CI = − 0.13 to 0.22)	1.08 (CI = 0.89 to 1.32)	0.08 (CI = − 0.11 to 0.28)	1.06 (CI = 0.87 to 1.30)	0.06 (CI = − 0.14 to 0.26)

further supports the dynamic adaptation of treatment strategies. As a patient's condition progresses, the model's predictive insights can inform necessary modifications to therapeutic interventions, ensuring that the treatment remains consistently aligned with the patient's current risk profile. This adaptability can enhance patient outcomes by providing timely interventions based on the latest prognostic data. In addition, we refrained from dichotomizing quantitative data (such as age, size, or Nottingham score of tumor grade) into two groups based on their median or a suggested threshold in order to prevent information loss. Also, several previous studies eliminated predictors that were shown to be statistically insignificant in univariable analysis. We chose not to adopt this data-driven strategy, as recommended in reference books [23, 24], to mitigate the overfitting bias. Instead, we selected a large number of predictors based on existing literature and the opinions of expert physicians.

Developing robust prediction models for breast cancer necessitates careful consideration of collinearity, a common issue when incorporating a large number of MRI, pathological, and clinical features. Collinearity arises when predictors are highly correlated, potentially leading to inflated variances and unreliable model estimates. To mitigate this challenge, we removed or changed the definition of predictors with high variance inflation factors. This approach balances the need to address collinearity while preserving the model level of informativeness. Clinically, the elimination of multicollinearity simplifies the use of model while reducing the likelihood of predictors being influenced by distortions of correlated variables. Nevertheless, many studies have failed to assess collinearity carefully in their methodology and analysis.

A decline in model performance is certain to happen during internal validation. However, the decrease in our model performance was inconsiderable (about 0.1 in each model). It did not change interpretation zones as AUCs in full, bootstrap, and leave-one-out method models still remained "good" for both survival and recurrence models, and the "good" AUCs support the use of models in clinical settings [25, 26]. Regarding all seven calibration plots, our models exhibit a precise fit with their internal validation assessments. Ideally, there are small deviations between the expected and observed values, especially in outcome probabilities lower than 30% (in most cases). Based on the decision curves, this prediction model is highly recommended throughout the entire range of 0 to 40% probability of death and recurrence. Referring to Fig. 4, if this model is applied to all patients who have, for instance, a 10% probability of recurrence, the test will result in a net benefit of 4 patients per 100 patients.

External validation and clinical applicability remain issues in training a prediction model. Shrinkage analysis addresses this problem and solves the effect of sample size bias. We suggest that clinical centers intending to implement our findings utilize the calculator based on the coefficients

Table 4 Odds ratios and coefficients based on bootstrap shrinkage method for 8, 5, and 3-year recurrence models

		8-year total recurrence shrinkage analysis		5-year total recurrence shrinkage analysis		3-year total recurrence shrinkage analysis	
		Odds ratio	Coefficient	Odds ratio	Coefficient	Odds ratio	Coefficient
HER 2 status		N/A	N/A	N/A	N/A	N/A	N/A
Chemotherapy		1.07 (CI = 0.66 to 1.72)	0.07 (CI = − 0.40 to 0.54)	1.22 (CI = 0.68 to 2.17)	0.19 (CI = − 0.37 to 0.77)	1.49 (CI = 0.56 to 3.96)	0.39 (CI = − 0.57 to 1.37)
Contralateral breast involvement		1.05 (CI = 0.69 to 1.61)	0.05 (CI = − 0.36 to 0.47)	0.95 (CI = 0.57 to 1.58)	− 0.04 (CI = − 0.54 to 0.45)	0.70 (CI = 0.33 to 1.50)	− 0.34 (CI = − 1.10 to 0.41)
Ethnicity	White	0.93 (CI = 0.52 to 1.67)	− 0.06 (CI = − 0.65 to 0.51)	1.15 (CI = 0.55 to 2.41)	0.14 (CI = − 0.59 to 0.88)	1.09 (CI = 0.38 to 3.06)	0.08 (CI = − 0.94 to 1.12)
	Black	0.84 (CI = 0.44 to 1.89)	− 0.16 (CI = − 0.80 to 0.46)	0.94 (CI = 0.42 to 2.06)	− 0.06 (CI = − 0.84 to 0.72)	0.93 (CI = 0.32 to 2.69)	− 0.07 (CI = − 1.13 to 0.99)
Hormonal therapy	Positive PR/ER and not received hormonal therapy	1.32 (CI = 0.77 to 2.26)	0.28 (CI = − 0.25 to 0.81)	1.50 (CI = 0.82 to 2.75)	0.41 (CI = − 0.19 to 1.01)	1.35 (CI = 0.62 to 2.96)	0.30 (CI = − 0.47 to 1.08)
	Positive PR/ER and received hormonal therapy	0.82 (CI = 0.56 to 1.21)	− 0.18 (CI = − 0.51 to 0.19)	0.76 (CI = 0.50 to 1.17)	− 0.26 (CI = − 0.68 to 0.15)	0.56 (CI = 0.33 to 0.94)	− 0.57 (CI = − 1.10 to − 0.05)
Lymphovascular invasion		1.14 (CI = 0.77 to 1.67)	0.13 (CI = − 0.25 to 0.51)	1.28 (CI = 0.84 to 1.97)	0.25 (CI = − 0.17 to 0.67)	1.72 (CI = 0.98 to 3.03)	0.54 (CI = − 0.01 to 1.10)
M status		0.69 (CI = 0.25 to 1.94)	− 0.35 (CI = − 1.37 to 0.66)	0.31 (CI = 0.06 to 1.58)	− 1.15 (CI = − 2.76 to 0.46)	N/A	N/A
Menstrual status		1.11 (CI = 0.69 to 1.79)	0.11 (CI = − 0.35 to 0.58)	1.21 (CI = 0.70 to 2.08)	0.19 (CI = − 0.34 to 0.73)	1.17 (CI = 0.58 to 2.37)	0.16 (CI = − 0.53 to 0.86)
Multicentrality		1.19 (CI = 0.85 to 1.66)	0.17 (CI = − 0.15 to 0.51)	1.27 (CI = 0.86 to 1.87)	0.24 (CI = − 0.14 to 0.63)	0.84 (CI = 0.50 to 1.41)	− 0.16 (CI = − 0.67 to 0.35)
N status		1.01 (CI = 0.68 to 1.50)	0.01 (CI = − 0.37 to 0.40)	0.93 (CI = 0.53 to 1.46)	− 0.06 (CI = − 0.51 to 0.38)	1.27 (CI = 0.70 to 2.31)	0.24 (CI = − 0.34 to 0.84)
Oophorectomy		0.88 (CI = 0.51 to 1.51)	− 0.12 (CI = − 0.65 to 0.41)	0.80 (CI = 0.42 to 1.52)	− − 0.22 (CI = − 0.86 to 0.42)	0.47 (CI = 0.17 to 1.27)	− 0.73 (CI = − 1.71 to 0.24)
Tumor response	Complete response	0.14 (CI = 0.03 to 0.56)	− 1.91 (CI = − 3.26 to − 0.56)	N/A	N/A	N/A	N/A
	Incomplete response	1.04 (CI = 0.67 to 1.62)	0.04 (CI = − 0.39 to 0.48)	0.98 (CI = 0.61 to 1.57)	− 0.01 (CI = − 0.48 to 0.45)	0.83 (CI = 0.44 to 1.55)	− 0.18 (CI = − 0.80 to 0.43)
Pectoral involvement		1.66 (CI = 0.76 to 3.61)	0.51 (CI = − 0.26 to 1.28)	2.20 (CI = 0.98 to 4.93)	0.79 (CI = − 0.01 to 1.59)	1.75 (CI = 0.63 to 4.89)	0.56 (CI = − 0.46 to 1.58)
Radiotherapy		0.95 (CI = 0.62 to 1.43)	− 0.04 (CI = − 0.46 to 0.36)	1.36 (CI = 0.83 to 2.25)	0.31 (CI = − 0.18 to 0.81)	2.10 (CI = 0.96 to 4.55)	0.74 (CI = − 0.03 to 1.51)
Skin/nipple involvement		1.07 (CI = 0.62 to 1.83)	0.07 (CI = − 0.46 to 0.60)	1.06 (CI = 0.59 to 1.91)	0.06 (CI = − 0.51 to 0.65)	1.48 (CI = 0.75 to 2.95)	0.39 (CI = − 0.28 to 1.08)
Surgery type	Lumpectomy	2.87 (CI = 0.98 to 8.38)	1.05 (CI = − 0.01 to 2.12)	3.16 (CI = 0.86 to 11.6)	1.15 (CI = − 0.14 to 2.45)	1.69 (CI = 0.41 to 7.00)	0.52 (CI = − 0.89 to 1.94)
	Mastectomy	3.00 (CI = 1.09 to 8.19)	1.09 (CI = 0.09 to 2.10)	3.57 (CI = 1.03 to 12.3)	1.27 (CI = 0.03 to 2.51)	2.33 (CI = 0.59 to 9.26)	0.84 (CI = − 0.52 to 2.22)
T status	T2	1.18 (CI = 0.81 to 1.71)	0.16 (CI = − 0.2 to 0.54)	1.11 (CI = 0.72 to 1.71)	0.10 (CI = − 0.31 to 0.53)	1.20 (CI = 0.67 to 2.15)	0.18 (CI = − 0.39 to 0.76)
	T3	1.22 (CI = 0.68 to 2.18)	0.20 (CI = − 0.37 to 0.78)	1.15 (CI = 0.61 to 2.15)	0.14 (CI = − 0.48 to 0.76)	1.75 (CI = 0.83 to 3.69)	0.56 (CI = − 0.17 to 1.30)
	T4	1.41 (CI = 0.61 to 3.29)	0.35 (CI = − 0.49 to 1.19)	1.60 (CI = 0.65 to 3.92)	0.47 (CI = − 0.42 to 1.36)	1.75 (CI = 0.83 to 3.69)	0.39 (CI = − 0.63 to 1.42)

Table 4 (continued)

	8-year total recurrence shrinkage analysis		5-year total recurrence shrinkage analysis		3-year total recurrence shrinkage analysis	
	Odds ratio	Coefficient	Odds ratio	Coefficient	Odds ratio	Coefficient
Surgery time	1.29 (CI = 0.85 to 1.95)	0.25 (CI = − 0.15 to 0.67)	1.59 (CI = 0.99 to 2.55)	0.46 (CI = 0.00 to 0.93)	1.34 (CI = 0.70 to 2.55)	0.29 (CI = − 0.34 to 0.93)
Size (cm)	1.07 (CI = 1.00 to 1.13)	0.06 (CI = 0.00 to 0.12)	1.06 (CI = 0.99 to 1.13)	0.06 (CI = 0.00 to 0.13)	1.05 (CI = 0.97 to 1.13)	0.05 (CI = − 0.02 to 0.12)
Volume (cm3)	1.00 (CI = 0.99 to 1.00)	0.00 (CI = 0.00 to 0.00)	1.00 (CI = 0.99 to 1.00)	0.00 (CI = 0.00 to 0.00)	0.99 (CI = 0.99 to 1.00)	0.00 (CI = 0.00 to 0.00)
Breast density (%)	1.00 (CI = 0.99 to 1.01)	0.00 (CI = 0.00 to 0.01)	0.99 (CI = 0.98 to 1.01)	0.00 (CI = − 0.01 to 0.01)	1.00 (CI = 0.99 to 1.02)	0.00 (CI = 0.00 to 0.02)
Tumor SER in pre-contrast phase	0.91 (CI = 0.45 to 1.84)	− 0.08 (CI = − 0.78 to 0.61)	1.31 (CI = 0.56 to 3.04)	0.27 (CI = − 0.56 to 1.11)	1.08 (CI = 0.38 to 3.04)	0.07 (CI = − 0.95 to 1.11)
Breast SER in pre-contrast phase	4.52 (CI = 0.23 to 86.1)	1.50 (CI = − 1.43 to 4.45)	0.74 (CI = 0.2 to 22.0)	− 0.29 (CI = − 3.68 to 3.09)	0.17 (CI = 0.00 to 9.36)	− 1.77 (CI = − 5.77 to 2.23)
Breast SER in post-contrast phase	0.34 (CI = 0.05 to 2.17)	− 1.06 (CI = − 2.89 to 0.77)	0.61 (CI = 0.07 to 4.79)	− 0.48 (CI = − 2.54 to 1.56)	2.99 (CI = 0.23 to 38.6)	1.09 (CI = − 1.46 to 3.65)
Tumor wash-in rate in pre-contrast phase	1.00 (CI = 0.99 to 1.00)	0.00 (CI = 0.00 to 0.00)	1.00 (CI = 0.99 to 1.00)	0.00 (CI = 0.00 to 0.00)	1.05 (CI = 0.97 to 1.13)	0.00 (CI = 0.00 to 0.00)
Breast wash-in rate in pre-contrast phase	0.99 (CI = 0.99 to 1)	0.00 (CI = 0.00 to 0.00)	0.99 (CI = 0.99 to 1.00)	0.00 (CI = 0.00 to 0.00)	0.99 (CI = 0.99 to 1.00)	0.00 (CI = 0.00 to 0.00)
Time to peak (ms)	0.82 (CI = 0.67 to 0.99)	− 0.19 (CI = − 0.39 to 0.00)	0.84 (CI = 0.67 to 1.05)	− 0.17 (CI = − 0.39 to 0.05)	1.00 (CI = 0.99 to 1.02)	− 0.03 (CI = − 0.31 to 0.23)
Age (year)	0.99 (CI = 0.97 to 1.01)	0.00 (CI = − 0.02 to 0.01)	0.99 (CI = 0.97 to 1.02)	− 0.00 (CI = − 0.02 to 0.02)	1.08 (CI = 0.38 to 3.04)	− 0.01 (CI = − 0.04 to 0.01)
Nottingham score	1.22 (CI = 1.07 to 1.39)	0.20 (CI = 0.07 to 0.33)	1.19 (CI = 1.03 to 1.39)	0.18 (CI = 0.03 to 0.33)	0.17 (CI = 0.00 to 9.36)	0.27 (CI = 0.06 to 0.48)

Table 5 Area under curve (AUC) of models

	8-year survival	5-year survival	3-year survival	2-year survival	8-year total recurrence	5-year total recurrence	3-year total recurrence
Full model	0.834 (CI = 0.809 to 0.858)	0.838 (CI = 0.812 to 0.861)	0.876 (CI = 0.853 to 0.897)	0.891 (CI = 0.869 to 0.910)	0.776 (CI = 0.748 to 0.803)	0.808 (CI = 0.780 to 0.834)	0.892 (CI = 0.869 to 0.913)
Leave-one-out method	0.740 (CI = 0.711 to 0.768)	0.741 (CI = 0.712 to 0.770)	0.788 (CI = 0.761 to 0.816)	0.783 (CI = 0.755 to 0.809)	0.678 (CI = 0.647 to 0.708)	0.696 (CI = 0.664 to 0.727)	0.769 (CI = 0.740 to 0.798)
Shrinkage	0.758 (CI = 0.700 to 0.811)	0.762 (CI = 0.703 to 0.816)	0.808 (CI = 0.746 to 0.860)	0.814 (CI = 0.733 to 0.878)	0.697 (CI = 0.644 to 0.742)	0.727 (CI = 0.672 to 0.780)	0.818 (CI = 0.742 to 0.874)

derived from the shrinkage analyses. Our calculator enables the estimation of individualized probabilities of mortality and recurrence for each patient. This risk assessment holds substantial value in choosing treatment strategies and facilitating informed discussions with patients.

Our study had limitations: (1) Despite the advantage of a large sample size, our study had small number of events. Particularly, we were unable to develop models for local recurrence and distal recurrence in our patients separately due to a limited number of occurrences. This limitation highlights the need for future studies to collect more detailed data on recurrence types, enabling the development of specific models that could provide more targeted insights into risk factors and predictive markers for each type of recurrence. (2) Our model relies on MRI data, restricting its applicability to patients who cannot undergo MRI scans due to claustrophobia, implanted medical devices, or other contraindications. (3) The use

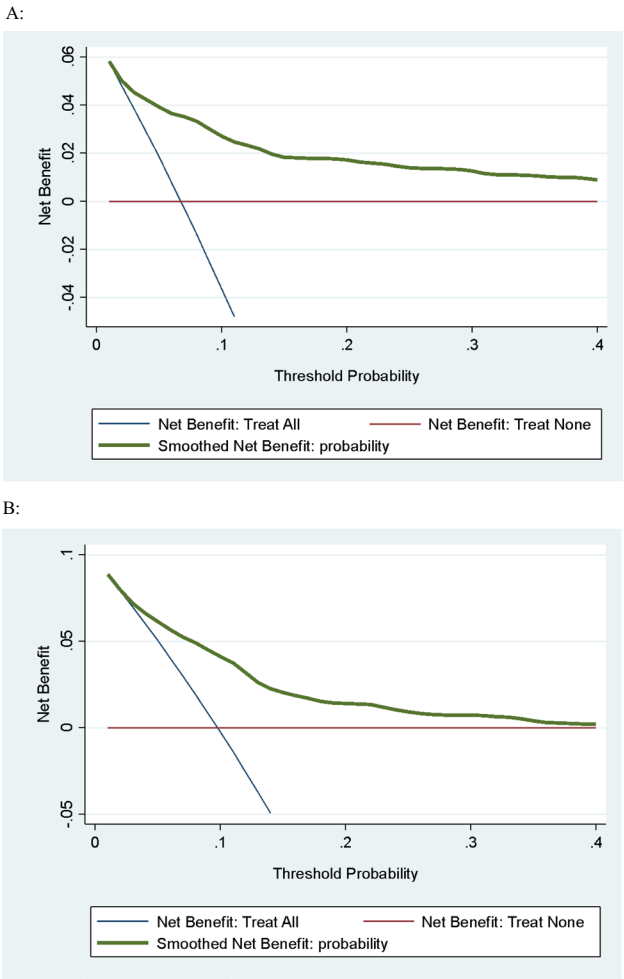


Fig. 4 **A** Survival decision-curve analysis plot. **B** Recurrence decision-curve analysis plot

of different annotation protocols by two separate radiologist groups may have introduced inter-reader variability. (4) Our study was designed at a single center, offering valuable insights but lacking external validation for our developed models. This limitation necessitates further research with multicenter cohorts to confirm the external validation of our results. However, the simplicity of our chosen predictors offers advantages for future studies aiming for broader validation while maintaining accessibility. (5) We omitted Ki- 67 expression levels and tumor pathology classification (IDC, ILC, metaplastic carcinoma, etc.) from our models due to high number of missing values in these variables. (6) Our investigation employed a retrospective design, focusing on analyzing existing data rather than prospectively following patients over time. (7) While artificial intelligence (AI) methods have become increasingly popular, they require extensive datasets and often lack transparency. In contrast, traditional regression approaches offer well-established, interpretable modeling. Consequently, this study employed conventional regression methods rather than AI techniques.

Conclusion

DCE-MRI parameters, along with pathological and clinical data, offer a comprehensive and simple model that accurately predicts the overall survival and recurrence of breast cancer patients. Our results suggest integrating the model into standard evaluation protocols for patients with breast cancer. Also, a probability calculator can serve as a guide for personalized patient treatment in healthcare provider centers.

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Author Contribution All authors contributed significantly to this article. A.Mohe: methodology, figures, statistical analysis, data collection. S.M: primary writer of manuscript, tables, data interpretation. A.Moha: providing revision for writing of manuscript, study design, validation. S.M.T: manager and principal investigator.

Data Availability The data that support the findings of this study are openly available in the cancer imaging archive (TCIA) at https://doi.org/https://doi.org/10.7937/TCIA.e3sv-re93.

Declarations

Informed Consent All participants provided written informed consent.

Animal Study N/A.

Conflict of interest The authors declare no competing interests.

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