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Original Article

A nomogram for predicting breast cancer based on hematologic and ultrasound parameters

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Abstract: Background: The aim of this study was to investigate the ultrasound and hematological indicators, subsequently utilizing them to predict breast cancer and construct predictive models and columnar plots. Methods: The clinical data of 200 patients with breast tumors receiving ultrasound and blood tests at Henan Provincial People's Hospital from January 2020 to January 2023 were collected. Patients were divided into training and validation sets at a 6:4 ratio using R language. Variables were screened using logistic regression, and a nomogram predicting breast cancer probability was constructed based on the training set. The predictive performance of the nomogram was evaluated in the validation set through receiver operating characteristic, calibration and decision curves. Model robustness was validated by bootstrap resampling. Results: Regression analysis revealed that maximum blood flow velocity within the breast mass ≥ 16.395 m/s, perfusion index ≥ 1.505, cancer antigen 15-3 ≥ 39.620 U/m, cancer antigen 125 ≥ 42.30 U/ml, carcinoembryonic antigen ≥ 6.520 ng/ml, Adler blood flow classification II & III, breast calcification present, and diameter of the lump > 2 cm were independent risk factors for breast cancer. Based on these ultrasonic parameters and blood indicators, the developed nomogram demonstrated excellent discrimination in both the training set (AUC = 0.917) and validation set (AUC = 0.844). The calibration plot showed high consistency between the nomogram-predicted and the actual results. Decision curve analysis indicated higher net benefit of this model. Conclusions: The nomogram developed in this study demonstrated solid predictive abilities for breast malignancy, indicating potential clinical value pending further research.

Keywords: Breast cancer, ultrasonic parameters, peripheral blood indicators, risk prediction model, nomogram

Introduction

Breast cancer remains a major health concern and research focus worldwide, greatly impacting the physical and mental health of women. Breast cancer has surpassed lung cancer as the most commonly diagnosed cancer and ranks 5th in cancer mortality [1, 2]. Early diagnosis and intervention are thus crucial for improving the outcomes of patients with breast cancer. In China, biopsy provides compelling evidence for early diagnosis [3], but has limitations in determining lymph node or distant metastasis. Moreover, the invasiveness and costs of biopsies restrict universal application.

Imaging examinations like mammography, ultrasound, and MRI are major breast cancer diagnostic tools that can complement biopsy limitations [4, 5]. These tools are non-invasive and provide detailed diagnostic information, with ultrasound being particularly cost effective. Ultrasound can obtain indicators like calcification, lesion diameter, and aspect ratio to assess the malignant potential of breast lesions. However, some studies have shown that the factors influencing breast cancer are multifaceted, and relying solely on ultrasound may miss early or minor lesions [6].

With advancements in blood testing, changes in certain blood markers have been associated with the development of breast cancer [7], including neutrophil-lymphocyte ratio (NLR) and cancer antigen 15-3 (CA15-3) [8, 9]. A combined approach of imaging and blood testing can be a more reasonable method with accuracy [10]. Li et al. developed a predictive model using only blood markers, yielding an area under the receiver operating characteristic curve (AUC) of 0.708 [11]. However, relying solely on blood may overlook the complexity of breast

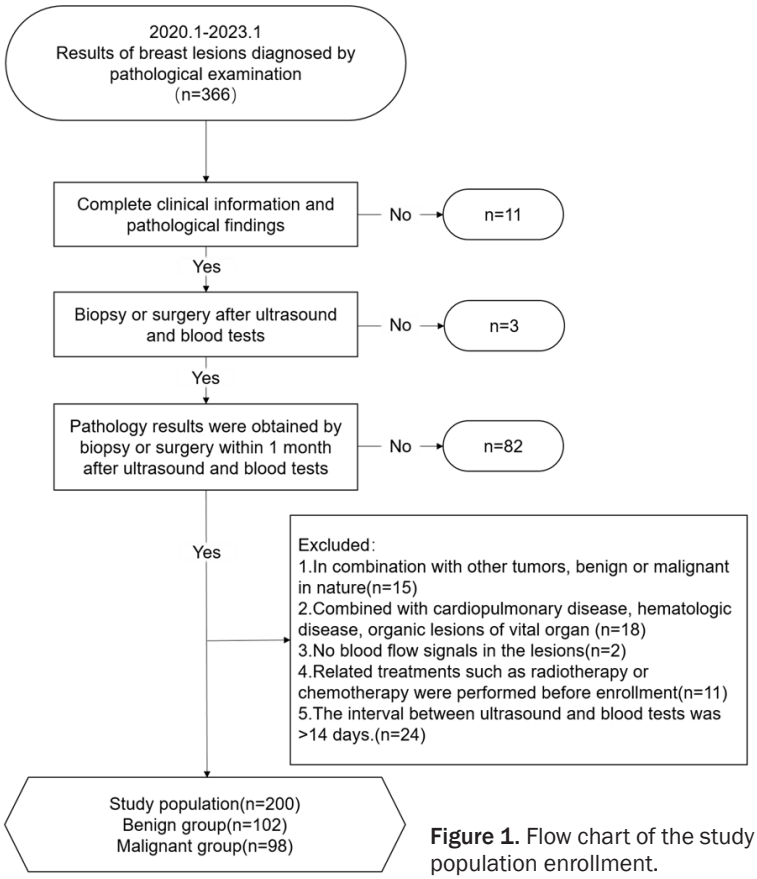

Figure 1. Flow chart of the study population enrollment.

cancer. Incorporating ultrasound parameters, which offer insights into tumor morphology, blood flow, etc., allows a comprehensive assessment when combined with blood markers.

Therefore, this study aimed to develop and validate a nomogram model utilizing widely accessible ultrasound and blood test parameters to predict early clinical diagnosis of breast cancer.

Material and methods

Patient characteristics

The study was approved by the Ethics Committee of Henan Provincial People's Hospital.

We collected data on female patients who underwent their first breast ultrasound and blood test from January 2020 to January 2023 at the Henan Provincial People's Hospital. These patients were eventually diagnosed by biopsy or surgery. The inclusion criteria were: (1) patients with complete and available clinical and pathological data; (2) patients who did not receive biopsy or surgery before ultrasound and blood tests. The exclusion criteria were: (1) patients with other tumors, benign or malignant; (2) patients with cardiopulmonary diseases; (3) patients with hematologic diseases; (4) patients with organic lesions of liver, kidney, heart, or brain; (5) patients without detected blood flow signals in the lesions; (6) patients who received treatments such as radiotherapy or chemotherapy before enrollment; (7) patients who underwent ultrasound and blood tests with an interval exceeded 14 days between the two procedures.

A total of 200 female patients with breast cancer meeting the inclusion/exclusion criteria (**Figure 1**) were included. The examination results categorized patients into a benign (n = 102) group and a malignant (n = 98) group, with no difference in relevant medical history between groups ($P < 0.05$). The mean age was (49.97 ± 11.65) years in the benign group and (50.07 ± 12.53) years in the malignant group. See **Table 1** for details.

Data collection

We collected the following patient information from electronic medical records or paper charts obtained during hospital consultations and examinations: (1) Demographic data: age, body mass index, age of menarche, menopausal status, hormone replacement therapy, family history of breast cancer. (2) Medical history: diabetes, hypertension. (3) Ultrasound parameters: Adler flow grading, breast calcification, lump diameter and aspect ratio, multiplicity, upper outer quadrant location, pulsatility index (PI) and resistive index (RI) of lump arteries, maximum intralesional blood flow velocity (Vmax). (4) Blood markers: liver and kidney function - total protein (TP), albumin (ALB), direct bilirubin (DBIL), total bilirubin (TBIL), aspartate amino-

Table 1. Comparison of observational indicators in the benign and malignant groups

Observation indicators	Benign group (n = 102)	Malignant group (n = 98)	$Z/t/\chi^2$	P
Age (year) [($\bar{x}$±s)]	49.97 ± 11.65	50.07 ± 12.53	0.059	0.953
BMI (kg/m^2) [(M, QR)]	22.2, 8.3	22.85, 8.2	0.848	0.396
Age of menarche ≥ Thirteen [n (%)]	19 (18.63)	11 (11.22)	2.148	0.143
Menopausal [n (%)]	21	30	1.677	0.195
History of diabetes [n (%)]	46	39	1.604	0.205
History of hypertension [n (%)]	61	55	0.941	0.332
Family history of breast cancer [n (%)]	14	22	2.577	0.108
History of estrogen use [n (%)]	29	34	0.908	0.341
Bloody nipple discharge [n (%)]	17	23	1.446	0.229
Spicule sign [n (%)]	39	49	2.807	0.094
Adler blood flow classification [n (%)]			4.424	0.035
0 & I	64	47		
II & III	38	51		
Breast calcification [n (%)]	40	58	3.973	0.046
Aspect ratio of the lump > 1 [n (%)]	39	51	3.849	0.050
Diameter of the lump (cm) [n (%)]			6.028	0.049
≤ 2	42	28		
3~5	40	37		
> 5	20	33		
Multiple lumps [n (%)]	26	31	0.925	0.336
The lump was located in the outer upper quadrant [n (%)]	39	43	0.658	0.417
Lump is irregular in shape [n (%)]	46	52	1.268	0.260
Suspicious lymphatic metastases [n (%)]	49	54	0.998	0.318
Mammary duct sprawl [n (%)]	62	66	0.934	0.33
PI [($\bar{x}$±s)]	1.50 ± 0.20	1.56 ± 0.21	2.356	0.019
RI [($\bar{x}$±s)]	0.78 ± 0.20	0.85 ± 0.20	2.520	0.013
Vmax (m/s) [($\bar{x}$±s)]	17.57 ± 4.40	19.22 ± 3.80	2.842	0.005
TP (g/L) [(M, QR)]	71.09, 11.53	72.22, 12.46	0.719	0.472
ALB (g/L) [(M, QR)]	45.80, 10.74	46.42, 9.85	0.004	0.997
DBIL (μmol/L) [(M, QR)]	5.73, 5.22	5.79, 5.06	0.171	0.864
TBIL (μmol/L) [(M, QR)]	11.45, 11.45	14.11, 8.24	0.360	0.718
AST (U/L) [(M, QR)]	19.78, 14.13	17.40, 18.99	0.719	0.472
ALT (U/L) [(M, QR)]	20.31, 17.21	17.57, 16.35	0.534	0.593
ALP (U/L) [(M, QR)]	70.12, 53.05	66.12, 55.43	0.211	0.833
GGT (U/L) [(M, QR)]	27.99, 26.63	29.48, 23.78	0.396	0.692
Blood glucose (mmol/L) [(M, QR)]	4.75, 1.84	4.74, 1.81	0.417	0.677
Creatinine (μmol/L) [(M, QR)]	81.00, 33.00	78.00, 36.00	0.515	0.607
UA (μmol/L) [(M, QR)]	164.50, 89.00	170.50, 100	0.067	0.946
TG (mmol/L) [(M, QR)]	1.63, 1.49	1.60, 1.46	0.087	0.931
TC (mmol/L) [(M, QR)]	3.90, 1.72	3.95, 2.25	0.722	0.470
LDL-C (mmol/L) [(M, QR)]	2.92, 1.07	2.99, 0.98	0.237	0.813
HDL-C (mmol/L) [(M, QR)]	1.52, 0.42	1.55, 0.59	0.066	0.947
ApoA1 (g/L) [(M, QR)]	1.48, 0.45	1.52, 0.55	0.847	0.397
ApoB (g/L) [(M, QR)]	1.58, 0.54	1.49, 0.50	1.028	0.304
CK (U/L) [(M, QR)]	71.28, 30.89	72.99, 30.52	0.073	0.942

LDH (U/L) [(M, QR)]	214.42, 98.37	212.02, 88.13	0.064	0.949
NLR [($\bar{x}$±s)]	3.19 ± 0.68	3.45 ± 0.90	2.284	0.024
RDW (%) [($\bar{x}$±s)]	14.80 ± 3.73	12.80 ± 3.14	4.097	< 0.001
CA15-3 (U/ml) [($\bar{x}$±s)]	30.71 ± 9.18	34.92 ± 8.60	3.345	0.001
CA125 (U/ml) [($\bar{x}$±s)]	36.78 ± 10.32	42.48 ± 12.40	3.529	0.001
CEA (ng/ml) [($\bar{x}$±s)]	6.27 ± 2.09	8.19 ± 2.09	6.527	< 0.001

PI: Perfusion index; RI: Resistance Index; Vmax: Maximum blood flow velocity within the breast mass; TP: Total Protein; ALB: Albumin; DBIL: Direct Bilirubin; TBIL: Total Bilirubin; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; ALP: Alkaline Phosphatase; GGT: γ-glutamyl transferase; UA: Uric Acid; TG: Triglycerides; TC: Total Cholesterol; LDL-C: Low-Density Lipoprotein Cholesterol; HDL-C: High-Density Lipoprotein Cholesterol; ApoA1: Apolipoprotein A1; ApoB: Apolipoprotein B; CK: Creatine Kinase; LDH: Lactate Dehydrogenase; NLR: Neutrophil-to-Lymphocyte Ratio; RDW: Red Cell Distribution Width; CA15-3: Cancer antigen 15-3; CA125: Cancer Antigen 125; CEA: Carcinoembryonic Antigen.

transferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), γ-glutamyl transferase (GGT), creatinine, uric acid (UA); lipid profile - triglycerides (TG), total cholesterol (TC), LDL-C, HDL-C, apolipoprotein A1 (ApoA1), apolipoprotein B (ApoB); myocardial markers - creatine kinase (CK), lactic dehydrogenase (LDH); inflammation markers - NLR, red cell distribution width (RDW); tumor markers - CA15-3, cancer antigen 125 (CA125), carcinoembryonic antigen (CEA). All blood samples were collected in the morning after overnight fasting.

Ultrasound and serum examinations

Ultrasound examinations were scheduled before or 3-7 days after the patient's menstrual period. Prior to the examinations, patients were calmed to maintain a stable and relaxed emotional state. Patients were instructed to breathe steadily throughout the procedure. The ultrasound was performed using an EPIQ Elite (China) color Doppler ultrasound machine with 4-18 MHz probes. Radial scans centered on the nipple assessed the breasts and axilla. Lesions were evaluated using BI-RADS standards for size, morphology, margins, axial ratio, calcification, and other characteristics. Adler grading was employed to determine the intralesional blood flow. Ultrasound findings were determined through consensus between two sonographers, each possessing over 10 years of experience.

Fasting blood samples were collected in the morning. The venous blood (20 mL) was centrifuged at 3000 rpm and 10 cm radial distance for 20 minutes. The serum was stored at -80°C. Testing procedures adhered to relevant instrument protocols. Glucose, creatinine, TP, ALB, DBIL, TBIL, AST, ALT, ALP, GGT, UA, TG, TC, LDL-C, HDL-C, and CK were measured using a Hitachi 7600 automated biochemical analyzer (Japan). CA15-3, CA125 and CEA were quantified by chemiluminescent immunoassay on a Roche E602 electrochemical luminescence analyzer (Switzerland). NLR and RDW were obtained using a Mindray BC-5390 automated hematology analyzer (China) with matched reagents.

Statistical methods

Data analysis was performed using SPSS 26.0 software. Normally distributed quantitative data were expressed as mean ± standard deviation ($\bar{x}$±s) and compared between groups by independent samples t-test. Non-normally distributed data were expressed as median and interquartile range (M, QR) and analyzed using nonparametric tests. Categorical data were expressed as frequencies and percentages (n, %) and compared between groups using chi-squared test. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated by logistic regression. Statistical significance was defined as $P < 0.05$. The primary outcome was the predictive performance of the nomogram, evaluated by area under the receiver operating characteristic curve (AUC) in both training and validation cohorts. The differences in AUCs were compared using the DeLong test. Secondary outcomes included identifying independent risk factors for breast cancer by logistic regression, and assessing the clinical utility

Table 2. Assignment of values

Observation indicators	Assign a value
Adler blood flow classification	0 & I = 0; II & III = 1
Breast calcification	Yes = 1; No = 0
Aspect ratio of the lump > 1	Yes = 1; No = 0
Diameter of the lump (cm)	≤ 2 cm = 1; 3-5 cm = 2; > 5 cm = 3
PI	1.505 < = 0; ≥ 1.505 = 1
RI	0.715 < = 0; ≥ 0.715 = 1
Vmax	16.395 m/s < = 0; ≥ 16.395 m/s = 1
NLR	3.475 < = 0; ≥ 3.475 = 1
RDW	13.990% < = 0; ≥ 13.990% = 1
CA15-3	39.620 U/ml < = 0; ≥ 39.620 U/ml = 1
CA125	42.30 U/ml < = 0; ≥ 42.30 U/ml = 1
CEA	6.520 ng/ml < = 0; ≥ 6.520 ng/ml = 1

PI: Perfusion index; RI: Resistance Index; Vmax: Maximum blood flow velocity within the breast mass; NLR: Neutrophil-to-Lymphocyte Ratio; RDW: Red Cell Distribution Width; CA15-3: Cancer antigen 15-3; CA125: Cancer Antigen 125; CEA: Carcinoembryonic Antigen.

of the nomogram using decision curve analysis.

Construction of a nomogram

To demonstrate the predictive value of the ultrasound parameters and blood indicators for breast cancer, a nomogram was constructed using the "rms" package in R (version 4.2.3) based on factors identified as significant by logistic regression analysis. Nomogram calibration was assessed using calibration curves. Decision curve analysis was applied to evaluate the feasibility of using these indicators to develop breast cancer prediction models.

To avoid overfitting and ensure generalizability, the samples were randomly divided into training and validation (6:4) sets. The training set was used for model development, while the validation set was used to assess the model performance. The DeLong test was used to compare ROC curves between training and validation sets to evaluate performance gaps.

Results

Clinical characteristics

Comparisons between malignant and benign groups revealed similar general demographic characteristics and medical histories (P > 0.05). However, PI, RI, and Vmax ultrasonographic parameters were significantly higher in the malignant group (P < 0.05). The malignant group also exhibited higher proportions of Adler grade II & III flow, breast calcification, lump diameter ≥ 3 cm, and axial ratio > 1 compared to the benign group (P < 0.05). Regarding blood indicators, the LNR and serum levels of CA15-3, CA125 and CEA were markedly higher, while the RDW was lower in the malignant group (P < 0.05). No significant intergroup differences were observed in other indicators (P > 0.05). See **Table 1** for details.

Univariate and multivariate regression analysis

The general data with significant difference between the two groups were included, and cutoff values were calculated for continuous. The indicators included in the regression analysis were assigned, as shown in **Table 2**. Using the training set, a prediction model was constructed. Univariate and multivariate regression analysis showed that Vmax ≥ 16.395 m/s, PI ≥ 1.505, CA15-3 ≥ 39.620 U/m, CA125 ≥ 42.30 U/ml, CEA ≥ 6.520 ng/ml, Adler blood flow classification II & III, presence of breast calcification, and diameter of the lump > 2 cm were independent risk factors for breast cancer (**Table 3**). CEA was the blood indicator with the greatest impact. In univariate analysis, when CEA ≥ 6.520 ng/ml, the risk of breast cancer increased 5.495-fold, and in multivariate regression analysis it increased 10.412-fold. For ultrasound indicators, PI and breast calcification showed the greatest impacts in univariate analysis. When PI > 1.505 or breast calcification was detected in a patient, the risk of breast cancer increased 3.323-fold and 2.981-fold, respectively. In multivariate analysis, breast calcification had the greatest impact, increasing the risk by a factor of 8.178-fold.

Development and validation of nomogram

A nomogram was developed to predict the probability that a patient's breast lump was malignant. With a total score of above 300, the patient would have over 50% probability of having breast malignancy (**Figure 2**). The analysis resulted in an AUC of 0.917 (95% *CI*: 0.864-

Table 3. Logistic regression results for training set

Observation indicators	Univariate logistic regression					Multifactor logistic regression				
	β	*Wald* χ^2	*OR*	*P*	95% *CI*	*B*	*Wald* χ^2	*OR*	*P*	95% *CI*
Adler blood flow classification	0.746	3.960	2.109	0.047	1.011~4.398	1.419	5.793	4.132	0.016	1.968~13.117
Breast calcification	1.092	8.294	2.981	0.004	1.418~6.270	2.101	11.463	8.178	0.001	0.474~27.603
Aspect ratio of the lump > 1	0.331	0807	1.392	0.369	0.676~2.865	0.376	.467	1.456	0.495	1.850~4.278
Diameter of the lump (cm)	0.449	3.198	1.567	0.074	0.958~2.565	0.910	4.777	2.486	0.029	0.957~5.623
PI ≥ 1.505	1.201	8.453	3.323	0.004	1.479~7.467	1.962	8.959	7.113	0.003	0.292~25.702
RI ≥ 0.715	0.803	3.994	2.232	0.046	1.016~4.906	0.443	0.531	1.557	0.466	2.390~5.118
Vmax ≥ 16.395 m/s	0.950	6.838	2.585	0.012	1.237~5.401	1.887	8.456	6.597	0.004	1.122~23.529
NLR ≥ 3.475	0.610	2.654	1.841	0.103	0.883~3.838	1.085	3.548	2.961	0.060	2.672~9.161
RDW (%) ≥ 13.990%	0.692	3.424	1.997	0.064	0.960~4.154	0.109	0.036	0.897	0.849	1.301~2.755
CA15-3 ≥ 39.620 U/ml	1.523	9.921	4.587	0.002	1.778~11.834	2.217	10.426	9.177	0.001	2.423~35.241
CA125 ≥ 42.30 U/ml	0.713	3.378	2.039	0.066	0.954~4.360	1.319	4.609	3.740	0.032	.495~12.468
CEA ≥ 6.520 ng/ml	1.704	16.292	5.495	< 0.001	2.402~12.568	2.343	11.401	10.412	0.001	1.099~40.569

PI: Perfusion index; RI: Resistance Index; Vmax: Maximum blood flow velocity within the breast mass; NLR: Neutrophil-to-Lymphocyte Ratio; RDW: Red Cell Distribution Width; CA15-3: Cancer antigen 15-3; CA125: Cancer Antigen 125; CEA: Carcinoembryonic Antigen.

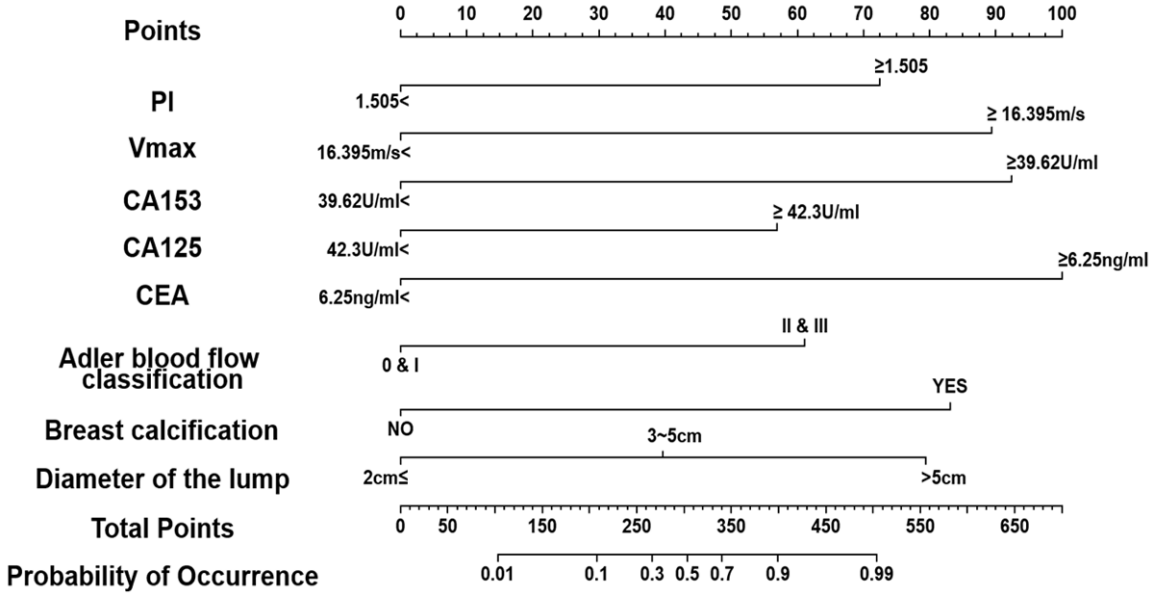

Figure 2. Nomogram based on ultrasonography parameters and blood indicators. PI: Perfusion index; Vmax: Maximum blood flow velocity within the breast mass; CA15-3: Cancer antigen 15-3; CA125: Cancer Antigen 125; CEA: Carcinoembryonic Antigen.

0.969) for the training set and 0.844 (95% *CI*: 0.761-0.927) for the validation set (**Figure 3A**, **3B**). We used the DeLong test to compare the two AUC values, which showed no statistically significant difference (P = 0.149), indicating minimal variation in model prediction capability between the training and validation sets. Both training and validation calibration curves demonstrated good calibration, where the predicted values closely matched the observed values (**Figure 3C**, **3D**). The decision curves of the training and validation sets showed that using the model to predict breast malignancy in patients can always lead to a higher net benefit than either intervening in all patients or not intervening in any patients (**Figure 3E**, **3F**).

Comparison of predictive models

We constructed another predictive model using only hematological risk factors and demographics from the training set, which resulted in an AUC of 0.768 (95% *CI*: 0.687-0.849) for the training set and an AUC of 0.727 (95% *CI*:

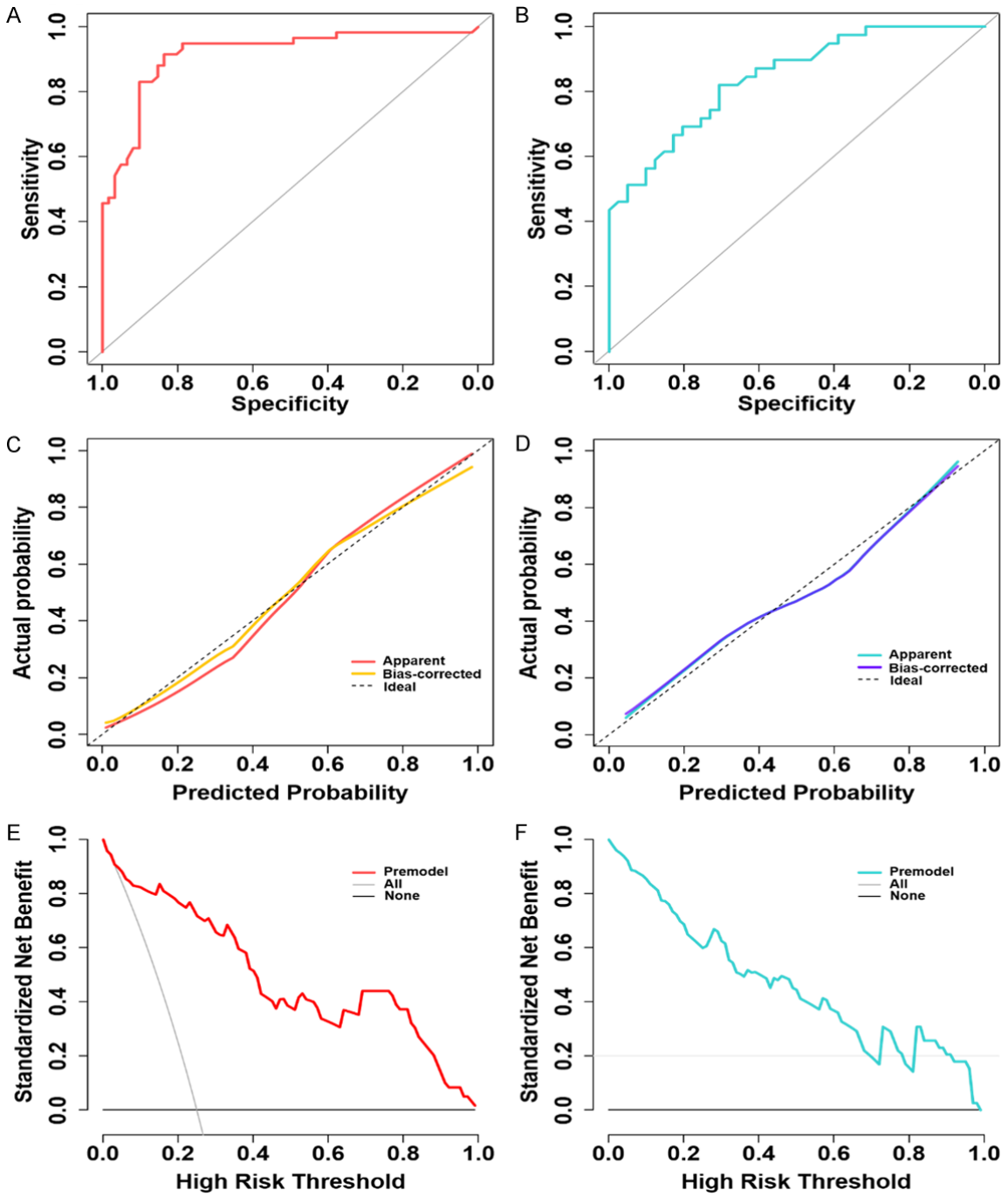

Figure 3. Validation of the predictive models based on blood indicators and ultrasonic indicators. A: Training set's receiver operating characteristic curve. B: Validation set's receiver operating characteristic curve. C: Training set's calibration curve. D: Validation set's calibration curve. E: Training set's decision curve. F: Validation set's decision curve.

0.619-0.835) for the validation set (**Figure 4A**, **4B**). The DeLong test showed no significant difference between the two AUC values (P = 0.552). The calibration curves also demonstrated good calibration of the model (**Figure 4C**, **4D**). The decision curve for the training set showed that using this model to predict breast cancer would yield higher net benefit across threshold probabilities 0.05-0.7, while decision curve for the validation set showed higher net

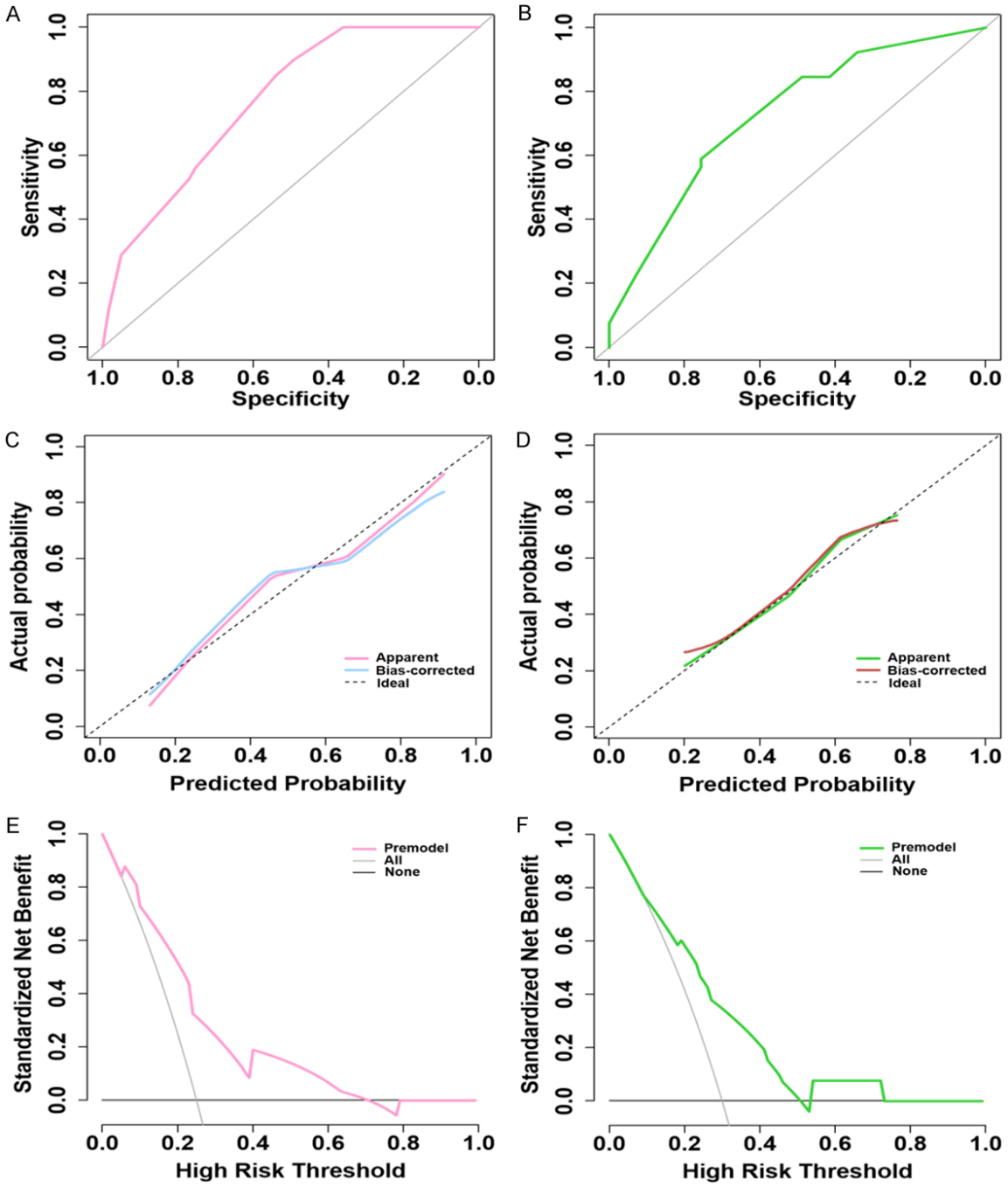

Figure 4. Validation of the predictive models based on blood indicators and demographics. A: Training set's receiver operating characteristic curve. B: Validation set's receiver operating characteristic curve. C: Training set's calibration curve. D: Validation set's calibration curve. E: Training set's decision curve. F: Validation set's decision curve.

benefit between the threshold probability ranges of 0.1-0.5 and 0.52-0.72 (**Figure 4E**, **4F**).

We compared the results between the two predictive models. The training and validation calibration curves for both models demonstrated good calibration, with high agreement between predicted and observed values. Using the DeLong test, the model incorporating ultrasound parameters and blood markers had significantly higher AUC values compared to the model using only hematological risk factors and de-

mographics (0.917 vs. 0.727, $P < 0.001$). The model with ultrasound and blood markers also had a wider threshold probability range for higher net clinical benefit, indicating overall better performance compared to the model using only hematological risk factors and demographics.

Discussion

Breast cancer is now the leading cause of cancer deaths in women globally, and the female population is facing financial burdens from coping with breast cancer. Nearly 700,000 women died of breast cancer in 2020 [12]. Primary prevention of breast cancer should be conducted by reducing exposure to known breast cancer risk factors. In low- and middle-income countries, early diagnosis and accessibility to treatment still need to be improved [13, 14]. In early screening, ultrasound is noninvasive, relatively affordable, and convenient. Integrating additional cost-effective and easily accessible diagnostic tools, such as blood tests, could enhance the accuracy of screening for malignant breast lesions, constituting a viable approach. Recent research has substantiated the viability of using blood tests to predict the presence of malignant breast lesions in patients with breast lumps [15], thus establishing a foundation for the current investigation. We constructed a nomogram based on ultrasound parameters and blood test indices to predict the likelihood of malignancy in patients with breast lumps, aiming to minimize unnecessary examinations which result in medical waste, economic and psychological burdens, and potential medical risks.

In this study, we identified eight variables, namely, IP, Vmax, Adler blood flow classification, breast calcification, diameter of the lump, CA15-3, CA125, and CEA, as the most significant predictive factors. By constructing a nomogram utilizing these variables, we were able to accurately identify patients with early malignant lesions, indicating a promising potential for clinical application. Our findings regarding the effectiveness of CA15-3, CA125, and CEA as predictors align with the results of Li et al., who also developed a promising nomogram incorporating other serum biomarkers (AUC = 0.708) [11]. Notably, our other model built solely using hematological risk factors and demographics exhibited comparable predictive performance (AUC = 0.727) to theirs. However, the incorporation of ultrasound parameters significantly enhanced its predictive ability (AUC = 0.917). Therefore, we assert that ultrasound parameters play a crucial role in the prediction of breast cancer.

Through case comparison, we discovered that the Vmax values in patients with malignant breast lesions typically exceeded those in patients with benign lumps, which aligns with the findings of Niu et al. [16]. This observation could be attributed to tumor angiogenesis and abnormal blood supply. For instance, the development of angiogenesis induced by tumors results in the formation of numerous distorted and dilated blood vessels, thereby increasing vascular density and blood flow to the tumor. Simultaneously, the walls of these newly generated tumor vessels are weak and immature, making them susceptible to vasodilation and consequently elevating the Vmax values [16, 17]. Larger masses often demand a greater blood supply, whereas benign masses such as adenomas tend to grow slowly with well-defined boundaries, making a significant increase in Vmax less likely. Conversely, malignant tumors exhibit rapid growth and require additional nutrients, necessitating not only an increased number of vessels but also faster flow speed within these vessels. Furthermore, during the expedited growth of malignant tumors, certain tumor cells are more prone to entering circulation through the accelerated flow in vessels, leading to a further dissemination of tumor cells in the patient [18]. Therefore, by combining current research perspectives, our study highlights the phenomena wherein the malignant group exhibited higher Vmax, Adler blood flow classification, and lump diameter compared to the benign group. These findings suggest that the potentially significant correlations among these three factors, contributing to their efficacy as predictive indicators.

In addition, breast calcification can be caused by tumor-secreted calcium salts [19]. Nevertheless, various factors can contribute to breast calcification, including tissue degeneration, necrosis, and deposition of calcium salts. Consequently, it is crucial to thoroughly investigate the characteristics of breast calcification, as it aids in the diagnosis of lesion nature.

Therefore, a meticulous analysis of calcification shape, number, location, and correlation with surrounding structures is warranted when a patient presents with breast calcification.

In blood tests, CA15-3, CA125, and CEA are commonly utilized a s tumor markers, with current research indicating that elevated levels of CA15-3 and CEA are associated with a higher tumor burden [20, 21]. This correlation can be attributed to the abundant expression and release of CA15-3 and CEA by tumor cells. Tumors with larger volumes often harbor a greater number of secreting tumor cells, leading to higher levels of CA15-3 and CEA compared to benign masses. CA125 is typically used as a marker for ovarian cancer, and its elevation in our subjects may be indicative of metastasis to the ovaries or other complications [22, 23]. Although effective in the nomogram, CA125's predictive value and mechanisms require further investigation to clarify its relationship with breast cancer. Several peripheral blood indices were taken into consideration due to research suggesting that breast cancer metastasis can affect organs such as lungs and liver [24, 25]. Changes in related indices might indirectly suggest lesion deterioration. However, these data did not reveal any significant differences between the malignant and benign groups in this study.

This study offers an effective prediction model that could act as an additional screening tool for high-risk breast cancer patients in clinical practice. However, further external validation and optimization are still necessary. As a retrospective study conducted at a single center, our conclusions may still carry a risk of bias. Due to our sample size and selective inclusion criteria, there may not have been significant differences in general demographic characteristics between the two groups. We highlighted comparable demographics between the groups to provide specificity for further analysis. This could lead to an underestimation of the predictive value of general demographic factors on breast cancer. As a result, there is a need for future multi-center studies with longer follow-ups to enhance the optimization of the included indices, and to develop a more dependable prediction model for clinical diagnosis.

Conclusion

The PI, Vmax, Adler blood flow classification, breast calcification, diameter of the lump, CA15-3, CA125, and CEA are effective predictors for breast cancer. A nomogram with a strong predictive performance and clinical utility for predicting malignant breast lesions was constructed and evaluated based on these effective predictors in this study. This nomogram can function as an auxiliary tool to screen high-risk patients.

Disclosure of conflict of interest

None.

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