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Nomogram for Predicting Chemotherapy-Induced Nausea and Vomiting for Breast Cancer Patients

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Chemotherapy-induced nausea and vomiting (CINV) is a common side effect of cancer treatment. The factors influencing CINV in breast cancer patients remain unclear. In this study, we developed a nomogram for predicting the occurrence of CINV in this group using prospective clinical data. We pooled data from multiple studies which focused on the emetogenic chemotherapy. Then, we collected 334 breast cancer patients at Hunan Cancer Hospital (training set) to analyze the demographic and clinical variables. Using multivariate logistic regression, we identified the five significant factors that were associated with CINV: history of CINV, chemotherapy regimen, chemotherapy cycle, metastasis, and symptoms of distress. Then, we construct a prediction nomogram. The external validation set comprised an additional 66 patients. The reliability of the nomogram was assessed by bootstrap resampling. The C-index was 0.78 (95% confidence interval [CI], 0.73-0.85) for the training set and 0.74 (95% CI, 0.62-0.85) for the validation set. Calibration curves showed good concordance between predicted and actual occurrence of CINV. In conclusions, our nomogram model can reliably predict the occurrence of CINV in breast cancer patients based on five significant variables, which might be useful in clinical decision-making.

Keywords: breast cancer; chemotherapy-induced nausea and vomiting (CINV); nomogram; predictive model; risk factors
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Introduction

Breast cancer is the most common cancer and the first leading cause of cancer-related death in women (Sung et al. 2021). Chemotherapy is one of the most important treatment options for breast cancer but chemotherapy-induced nausea and vomiting (CINV) is a major side effect (Mellin et al. 2018), with a reported incidence as high as 40%. Severe nausea and vomiting not only cause physical and psychological trauma to the patient, but can also reduce their treatment adherence. Antiemetic drugs are increasingly being prescribed by doctors, but current recommendations are based on the emetogenicity of chemotherapeutic agents (Roila et al. 2010; Hesketh et al. 2017) irrespective of individual patients' conditions. Clinicians often underestimate the incidence of nausea, which is not as well controlled as emesis (Rapoport 2017). It is therefore critical to develop a personalized approach to the management of CINV based on individual risk prediction, which could guide more effective antiemetic prophylaxis prior to chemotherapy.

Although there are predictive models for CINV (Dranitsaris et al. 2009; Petrella et al. 2009; Bouganim et al. 2012; Dranitsaris et al. 2013), they are not specific to a cancer type and have shortcomings, including limited clinical applicability and validity in real-world settings. One

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multilevel logistic regression model was established to predict CINV based on prospective data from 3 chemotherapy cycles, but had low accuracy (Molassiotis et al. 2013). The selection of variables of interest in the model is not based on the results of multivariable analysis, but based on common risk factors. In addition, the study population included in the model was targeted at patients receiving moderate/high emetic chemotherapy regimens, and patients who receive first-time chemotherapy. This study also did not cover the multi cycle observation population. Importantly, the accuracy of the model is not ideal (Hu et al. 2016).

Mathematical models have been widely used to predict the risk of diseases or symptoms (Rivaz et al. 2019; Zhang et al. 2020). A nomogram not only integrates multiple prediction variables (Kattan 2002) but can also accurately predict the probability of an individual event. In the present study, we developed and externally validated a nomogram for predicting the occurrence of CINV in breast cancer patients receiving chemotherapy.

Materials and Methods

Study design

This study used a prospective, longitudinal, observational design over 2 cycles of chemotherapy. Considering the effectiveness of the final model, in this study, we only reported the results of the first round of data.

Study population

Breast cancer patients were recruited from 2 different hospitals in Hunan Province, China. Data for 420 patients were available. The inclusion criteria were as follows: 1) definitive diagnosis of breast cancer; 2) ≥ 18 years old; 3) about to receive highly, moderately and lower emetogenic chemotherapy; 4) volunteered to participate in this study; and 5) female. The exclusion criteria were as follows: 1) impaired cognitive function or communication skills; 2) unaware of their disease; 3) diagnosed with a chronic digestive or other serious systemic disease; 4) using opioids; 5) participating in other breast cancer studies; and 6) experiencing nausea and vomiting caused by factors other than chemotherapy, such as radiotherapy.

Informed consent and ethical approval

Informed consent was obtained from all individual participants included in the study. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study had been approved by the Medical Ethics Committee of Hunan Cancer Hospital. The reference number is 2019-21.

Measurement tools

We used four measurement tools in this study. The questionnaire of factors related to CINV in breast cancer patients had four parts: (1) general information [age, body mass index (BMI), education level, etc.]; (2) patients' history (incidence of CINV in the previous cycle, drinking, smoking, reaction during pregnancy, motion sickness, sleep time before chemotherapy, etc.); (3) disease factors (disease stage, pathologic type, metastasis, etc.); and (4) drug factors (chemotherapy regimen, number of chemotherapy cycles, and antiemetic regimen). The second instrument was the Multinational Association of Supportive Care in Cancer (MASCC) Antiemesis Tool (MAT). This self-rating scale, which included 8 items on 2 subscales, assessed the occurrence of CINV through face-to-face or telephone interviews on days 2 and 6 after chemotherapy. The third tool was the Chinese version of the Generalized Anxiety Scale (He et al. 2010), which evaluated the severity of anxiety symptoms based on seven items. The last tool was Symptom Distress Scale (McCorkle and Young 1978). We used the Symptom Distress Scale to measure this variable. This was a widely-used 13-item scale which measured the symptom distress for the frequency of nausea, the intensity of nausea, appetite, insomnia, the frequency of pain, the intensity of pain, fatigue, bowel pattern, concentration, appearance, outlook, breathing, and cough. The content validity index of the scale was 0.90, and the internal reliability was between 0.66 and 0.85. The reliability and validity of the scale were good.

Identification of factors influencing the occurrence of CINV

We examined whether any of the following demographic and clinical variables could predict CINV occurrence: age, education, marital status, working conditions, performance status (PS), BMI, smoking, alcohol consumption, history of motion sickness, history of constipation, sleep time before chemotherapy, history of CINV, over-the-counter medications at home, symptoms distress, anxiety, history of hypertension, history of diabetes, chronic renal insufficiency, history of coronary heart disease, disease stage, metastasis, pathologic pattern, chemotherapy regimen, number of chemotherapy cycles and antiemetic drug regimen.

Based on the occurrence of CINV, patients were divided into CINV group and non-CINV group. Alcohol consumption was defined as the average consumption of an alcoholic beverage larger than one time per week. Chemotherapy agents were classified as highly emetogenic chemotherapy (emetic risk > 90%, HEC), moderately emetogenic chemotherapy (emetic risk 30%-90%, MEC), low emetogenic chemotherapy (emetic risk 10%-30%, LEC) and minimal emetogenic chemotherapy (emetic risk < 10%) according to National Comprehensive Cancer Network (NCCN Guidelines Version 2.2020 Antiemesis). In our study, HEC including AC (anthracycline cyclophosphamid) combination defined as any chemotherapy regimen that contains an anthracycline and cyclophosphamid, carboplatin AUC ≥ 4, epirubicin > 90 mg/m^2, doxorubicin ≥ 60 mg/m^2; MEC including cyclophosphamid ≤ 1,500 mg/m^2,

doxorubicin < 60 mg/m^2, epirubicin ≤ 90 mg/m; LEC including navelbine, TAX (taxol), xeloda, gemcitabine and docetaxel. (LEC and MEC were combined as there was no statistically significant difference between these categories). Antiemetic drug regimens were classified as single-agent (5-HT3 receptor antagonist), doublet (5-HT3 receptor antagonist + corticosteroid), and triplet (5-HT3 receptor antagonist + corticosteroid + neurokinin-1 receptor antagonist).

Many other factors can increase the risk of CINV such as the expectation of CINV before chemotherapy, social functioning, neurotransmitter levels, etc. However, these factors are subjective or not amenable to measurement, and were therefore excluded from our model.

Outcome indicators

The presence or absence of overall CINV in breast cancer patients was outcome indicators. Overall CINV was defined as the occurrence of acute (Nausea or vomiting occurring within 24 h after chemotherapy) or delayed CINV (Nausea or vomiting occurring between 24 h and 7 days after chemotherapy).

Statistical analysis

SPSS v24.0 software (SPSS Inc, Chicago, IL, USA) was used to input and analyze the survey data. Demographic data of patients and the incidence of CINV were presented by frequency and percentage. The comparison of baseline data between the training group and the validation group was performed using the chi-square test and rank sum test.

The presence or absence of CINV in breast cancer patients was the dependent variable and CINV-related factors were the independent variables in the univariate logistic regression analysis ($P < 0.10$); the independent variables were then incorporated into the multifactor analysis model by stepwise logistic regression to obtain the regression equation, which was used to identify factors with a P-value < 0.05.

Before establishing the nomogram, the prediction results were verified by bootstrap self-sampling. The training dataset was resampled 1,000 times for internal verification. Samples from another hospital were used for external validation. The predictive accuracy (discriminatory power) of the nomogram was evaluated based on the concordance (C-) index and receiver operator characteristic (ROC) curve analysis. A calibration plot was drawn to determine how

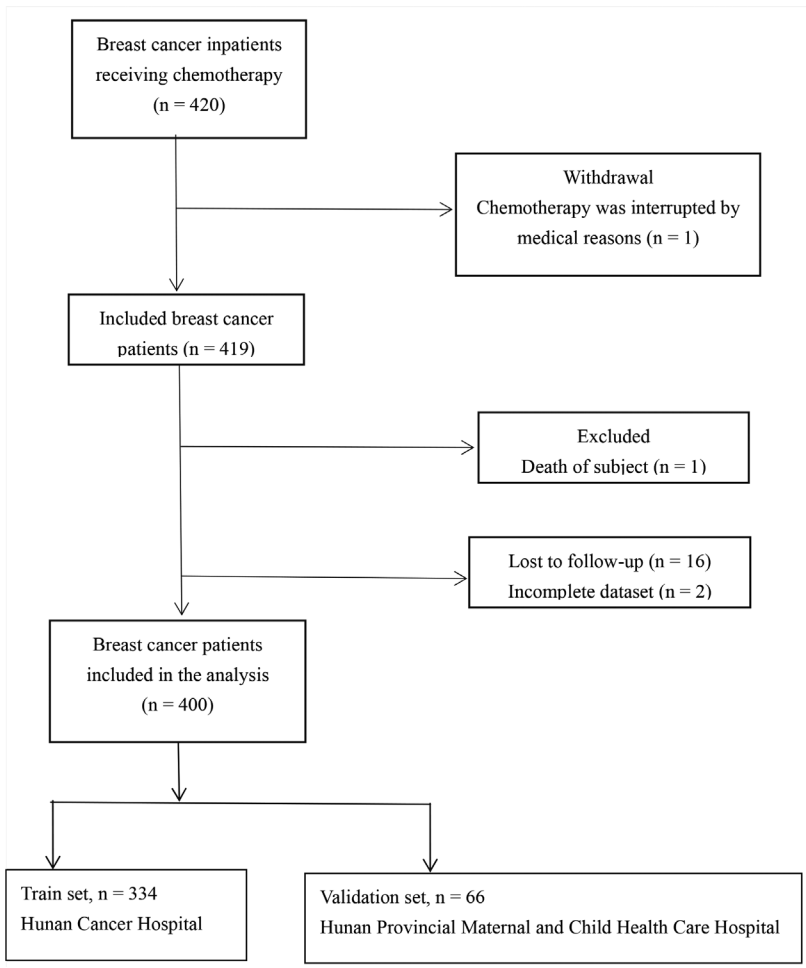

Fig. 1 Patients' flowchart.

Table 1. Demographic and clinical characteristics of the training and external validation sets.

Variable	Training set (n = 334)		External validation set (n = 66)		*P* value
	n	%	n	%	
Age, years					0.073
≤ 50	157	47.0	40	60.6	
> 50	177	53.0	26	39.4	
Education					0.927
Primary school or below	144	43.1	29	43.9	
Junior high school	130	38.9	25	37.9	
High school or technical secondary school	23	6.9	5	7.6	
Junior college and above	37	11.1	7	10.6	
Marital status					0.262
Married	324	97.0	62	93.9	
Other	10	3.0	4	6.1	
PS					0.211
0	91	27.2	14	21.2	
1	171	51.2	50	75.8	
≥ 2	72	21.6	2	3.0	
BMI					0.898
< 18.5	10	3.0	2	3.0	
18.5-23.9	183	54.8	37	56.1	
24-27.9	117	35.0	19	28.8	
≥ 28	24	7.2	8	12.1	
History of motion sickness					0.053
Yes	170	49.1	25	37.9	
No	164	50.9	41	62.1	
History of constipation					0.070
Yes	114	34.1	15	22.7	
No	220	65.9	51	77.3	
Sleep < 7 h before chemotherapy					0.390
Yes	161	51.8	28	57.6	
No	173	48.2	38	42.4	
History of CINV					0.534
Yes	130	38.9	23	34.8	
No	204	61.1	43	65.2	
Working conditions					0.712
Yes	30	9.0	5	7.6	
No	304	91.0	61	92.4	
History of smoking					0.092
Yes	4	1.2	3	4.5	
No	330	98.8	63	95.5	
History of drinking					0.500
Yes	13	3.9	4	6.1	
No	321	96.1	62	93.9	
Over-the-counter medications at home					0.751
Yes	17	5.1	2	3.0	
No	317	94.9	64	97.0	
Symptoms distress					0.320
Yes	209	62.6	37	56.1	
No	125	37.4	29	43.9	

Anxiety					0.914
Yes	99	29.6	20	30.3	
No	235	70.4	46	69.7	
History of hypertension					0.205
Yes	44	13.2	5	7.6	
No	290	86.8	61	92.4	
History of diabetes					0.486
Yes	18	5.4	5	7.6	
No	316	94.6	61	92.4	
Chronic renal insufficiency					0.529
Yes	2	0.6	0	0.0	
No	332	99.4	66	100.0	
History of coronary heart disease					0.379
Yes	10	3.0	0	0.0	
No	324	97.0	66	100.0	
Disease stage					0.333
I	57	17.1	10	15.2	
II	133	39.8	33	50.0	
III	108	32.3	19	28.8	
IV	36	10.8	4	6.1	
Metastasis					0.513
Yes	193	57.8	41	62.1	
No	141	42.2	25	37.9	
Antiemetic drug regimen					0.080
Single agent	86	25.7	9	13.6	
Doublet	126	37.7	32	48.5	
Triplet	122	36.5	25	37.9	
Pathologic pattern					0.656
Invasive non-specific carcinoma	308	92.2	56	84.8	
Other	26	7.8	10	15.2	
Chemotherapy target regimen					0.583
LEC/MEC	154	46.1	28	42.4	
HEC	180	53.9	38	57.6	
No. of chemotherapy cycles					0.503
< 3	207	62.0	38	57.6	
≥ 3	127	38.0	28	32.4	
Incidence of CINV*					
Acute CINV	93	27.8	26	39.4	0.061
Delayed CINV	84	25.1	10	15.2	0.142
Overall CINV	137	41.0	30	45.5	0.504

*Incidence of CINV in the training and external validation sets.
CINV, chemotherapy-induced nausea and vomiting; PS, performance status; HEC, highly emetogenic chemotherapy, including cis-platinum, pharmorubicin; MEC, moderately emetogenic chemotherapy, including cyclophosphamide + doxorubicin; LEC, low emetogenic chemotherapy, including navelbine, TAX (taxol), xeloda, gemcitabine and docetaxel; Single agent, 5-HT3 receptor antagonist; Doublet, 5-HT3 receptor antagonist + corticosteroid; Triplet, 5-HT3 receptor antagonist + corticosteroid + neurokinin-1 receptor antagonist.

well the probabilities predicted by the nomogram matched actual probabilities. Nomogram construction and validation was performed using the *rms* package of R 3.5.2 software (https://cran.r-project.org/bin/windows/base/old/3.5.2/). In all statistical analyses, $P < 0.05$ was considered significant.

Results

Characteristics of the study population

In total, 420 subjects were initially recruited but 20 subjects were subsequently excluded from the analysis: one patient's chemotherapy was interrupted, data were incom-

Table 2. Univariate logistic regression analysis of CINV in breast cancer.

Variable	Statistics n (%)	OR	95% CI	*P* value
Age, years				
≤ 50	157 (47.0)	Ref		
> 50	177 (53.0)	1.557	0.833-2.910	0.165
Education				0.717
Primary school or below	144 (43.1)			
Junior high school	130 (38.9)	0.711	0.388-1.305	0.271
High school or technical secondary school	23 (6.9)	0.984	0.290-1.337	0.980
Junior college and above	37 (11.1)	1.001	0.364-2.750	0.999
Marital status				
Married	324 (97.0)	Ref		
Other	10 (3.0)	4.062	0.813-20.286	0.088
PS				0.216
0	91 (27.2)			
1	171 (51.2)	1.149	0.572-2.307	0.697
≥ 2	32 (21.6)	0.586	0.242-1.421	0.237
BMI				0.518
< 18.5	10 (3.0)			
18.5-23.9	183 (54.8)	3.567	0.559-22.767	0.179
24-27.9	117 (35)	2.945	0.452-19.201	0.259
≥ 28	24 (7.2)	2.363	0.286-19.545	0.425
History of motion sickness				
Yes	170 (50.9)	Ref		
No	164 (49.1)	1.3	0.703-2.245	0.440
History of constipation				
Yes	114 (34.1)	Ref		
No	220 (65.9)	1.142	0.638-2.043	0.656
Sleep < 7 h before chemotherapy				
Yes	161 (48.2)	Ref		
No	173 (51.8)	0.751	0.421-1.341	0.334
History of CINV				
Yes	130 (38.9)	Ref		
No	204 (61.1)	6.158	3.045-12.453	< 0.001
Working conditions				
Yes	30 (9.0)	Ref		
No	304 (91.0)	0.461	0.161-1.325	0.151
History of smoking				
Yes	4 (1.2)	Ref		
No	330 (98.8)	0.192	0.013-2.907	0.234
History of drinking				
Yes	13 (3.9)	Ref		
No	321 (96.1)	1.766	0.446-6.993	0.418
Over-the-counter medications at home				
Yes	17 (5.1)	Ref		
No	317 (94.9)	1.406	0.403-4.905	0.593
Symptom Distress				
Yes	209 (62.6)	Ref		
No	125 (37.4)	3.225	1.748-5.950	< 0.001

Anxiety				
Yes	99 (29.6)	Ref		
No	235 (70.4)	1.437	0.774-2.670	0.251
History of hypertension				
Yes	44 (13.2)	Ref		
No	290 (86.8)	0.764	0.315-1.850	0.550
History of diabetes				
Yes	18 (5.4)	Ref		
No	316 (94.6)	3.030	0.811-11.325	0.099
Chronic renal insufficiency				
Yes	2 (0.6)	Ref		
No	332 (99.4)	0.578	0.016-21.381	0.766
History of coronary heart disease				
Yes	10 (3.0)	Ref		
No	324 (97.0)	1.053	0.212-5.236	0.949
Disease stage				0.386
I	57 (17.1)			
II	133 (39.8)	1.903	0.797-4.547	0.147
III	108 (32.3)	1.564	0.599-4.081	0.361
IV	36 (10.8)	0.983	0.270-3.574	0.979
Metastasis				
No	193 (57.8)	Ref		
Yes	141 (42.2)	0.257	0.132-0.503	< 0.001
Antiemetic drug regimen				0.258
Single agent	86 (25.7)			
Doublet	126 (37.7)	0.688	0.324-1.461	0.330
Triplet	122 (36.6)	0.511	0.230-1.136	0.100
Pathologic pattern				
Invasive non-specific carcinoma	308 (92.2)	Ref		
Other	26 (7.8)	2.013	0.735-5.514	0.174
Chemotherapy regimen				
LEC/MEC	154 (46.1)	Ref		
HEC	180 (53.9)	6.120	3.147-11.900	< 0.001
No. of chemotherapy cycles				
< 3	207 (62.0)	Ref		
≥ 3	127 (38.0)	0.444	0.223-0.884	0.021

plete for two patients, 16 patients were lost follow-up on day 6 and one patient died. Thus, 400 patients with complete data were ultimately included in the study (334 for nomogram development and 66 for validation), as shown in Fig. 1. The demographic and clinical characteristics of the study population for cycle 1 are shown in Table 1.

In the training set, CINV was reported in 41.0% of patients (137/334), with 27.8% (93/334) acute and 25.1% (84/334) delayed cases. In the validation set, 45.5% of patients (30/66) experienced CINV, including 39.4% (26/66) acute and 15.2% (10/66) delayed episodes.

Identification of risk factors related to CINV in breast cancer patients

We first assessed the predictive value of each variable by logistic regression analysis. Table 2 described univariate logistic regression analysis of CINV in breast cancer. Table 3 listed the result of multivariate logistic regression analysis. The factors most closely related to CINV were a history of CINV, symptom distress, metastasis, chemotherapy cycle and chemotherapy regimen; these were used for nomogram development. Notably, the age, which is an important predictor of CINV in cancer patients (Mosa et al. 2020), showed no significant association with the occurrence of CINV in our cohort.

CINV nomogram construction

We constructed a nomogram based on the logistic regression model developed using data from our training set. Significant risk factors identified by logistic regression analysis were fitted into the model. The final nomogram was shown in Fig. 2.

Table 3. Variables significantly associated with CINV from the multivariate logistic regression model.

Variable	B	OR	95% CI	*P* value
History of CINV				
No	Ref			
Yes	1.644	5.178	2.772-9.672	< 0.001
Symptoms Distress				
No	Ref			
Yes	1.017	2.765	1.605-4.763	< 0.001
Metastasis				
No	Ref			
Yes	−1.153	0.316	0.184-0.542	< 0.001
No. of chemotherapy cycles				
< 3	Ref			
≥ 3	−0.764	0.466	0.249-0.870	0.016
Marital status				
Married	Ref			
Other	1.406	4.079	0.921-18.061	0.064
Chemotherapy regimen				
LEC/MEC	Ref			
HEC	1.448	4.253	2.489-7.267	< 0.001

CI, confidence interval; CINV, chemotherapy-induced nausea and vomiting; HEC, highly emetogenic chemotherapy; LEC, low emetogenic chemotherapy; MEC, moderately emetogenic chemotherapy; OR, odds ratio; Ref, reference.

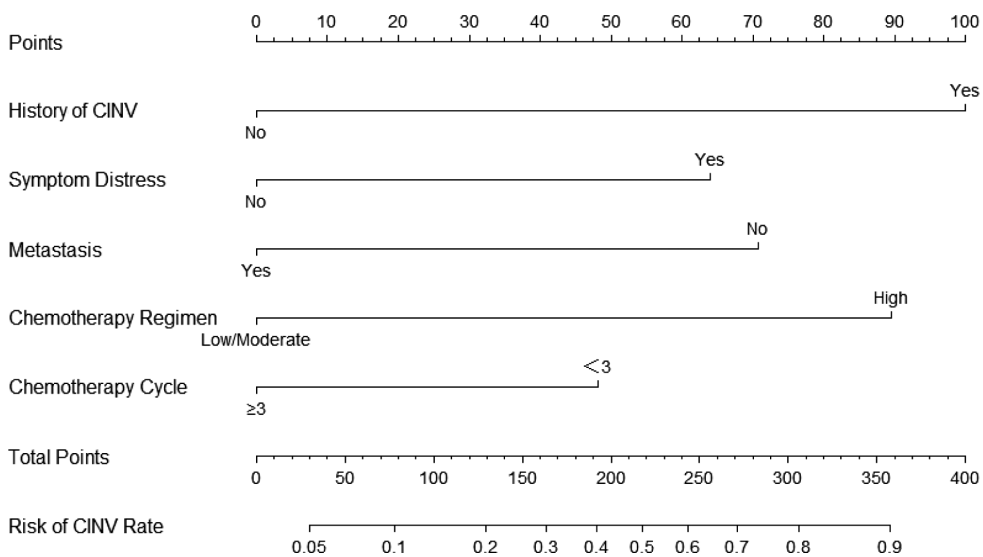

Fig. 2. Prediction nomogram of CINV in breast cancer patients receiving chemotherapy treatment. Low/moderate, low/moderately emetogenic chemotherapy; High, highly emetogenic chemotherapy.

Validation was first performed with the training set. The C-index for CINV prediction was 0.78 (95% CI, 0.73-0.83) in this nomogram; the area under the ROC curve (AUC) was 0.78 (95% CI, 0.73-0.83) (Fig. 3C), indicating a good discriminatory power. Bootstrapping (1,000 replications) was applied and a calibration curve was generated (Fig. 3A). There was no obvious deviation between the risk curve predicted by the model and actual observed risk, indicating that the model was well calibrated.

External validation of the CINV nomogram

Clinical data of patients (n = 66) from Hunan Provincial Maternal and Child Health Care Hospital were used for model validation. The calibration plot for the probability of CINV revealed good concordance between the nomogram prediction and actual observations (Fig. 3B). The C-index for CINV prediction was 0.74 (95% CI, 0.62-0.85) and the AUC was 0.71 (95% CI, 0.58-0.84), demonstrating that the nomogram was well fitted (Fig. 3D).

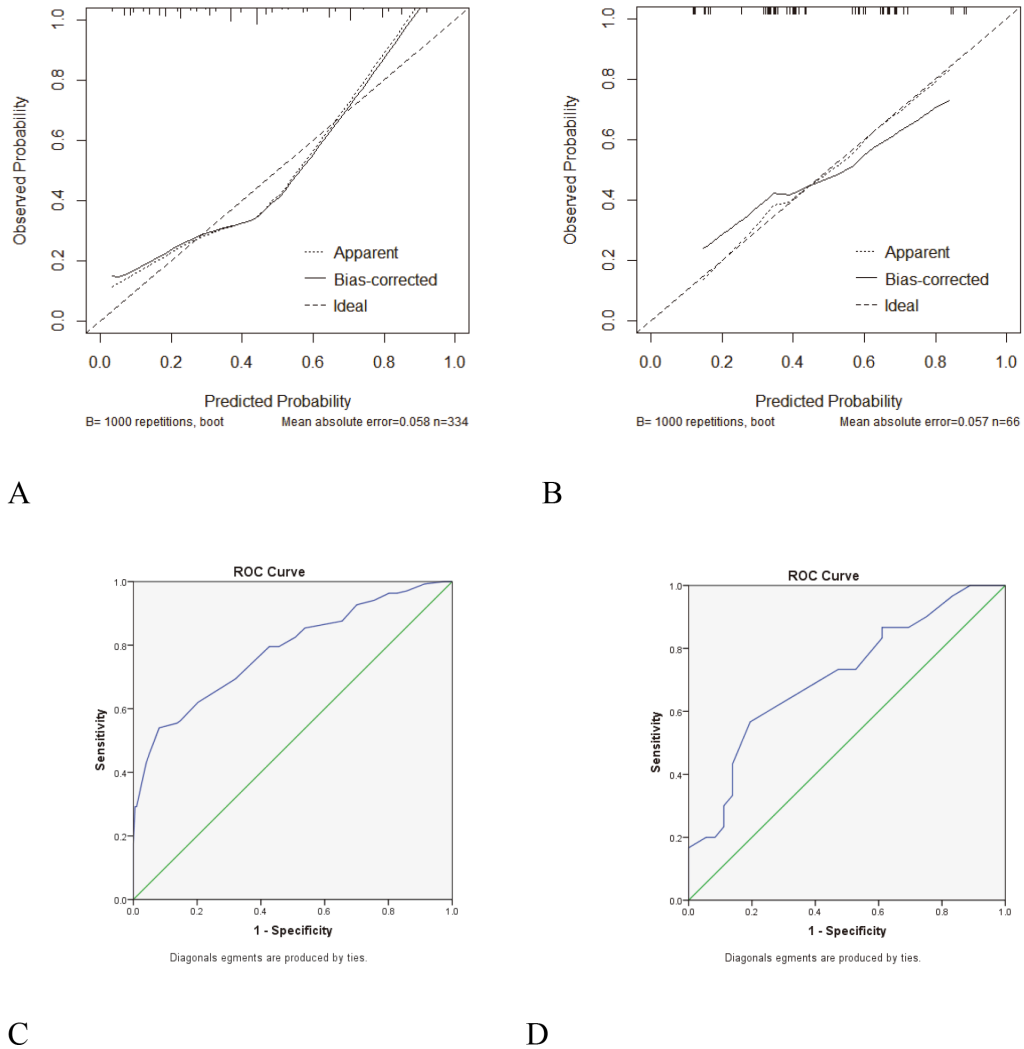

Fig. 3. Calibration plot and ROC curve of nomogram.
(A) Training set. (B) External validation set. The X axis shows the predicted CINV probabilities estimated with the nomogram, and the Y axis shows the actual rates of CINV. The solid straight line is the ideal reference line where predicted CINV corresponds to actual outcome, and the dashed straight lines represent a 10% margin of error. (C, D) ROC curve for discrimination in the training and validation cohorts; the AUC was 0.78 (95% CI, 0.73-0.83) and 0.71 (95% CI, 0.58-0.84), respectively, indicating that the model has good predictive value.

Discussion

We developed and validated a tool for predicting the risk of CINV in breast cancer patients. This tool has a graphical interface and is thus easy to use; individual patients' CINV risk can be determined without complex mathematical calculations. Although general antiemetic guidelines are important for preventing CINV, a personalized assessment of risk can help clinicians better manage this common adverse event (Clemons 2018; Warr 2018), for instance by prescribing appropriate antiemetics or selecting specific chemotherapy regimens. In addition to factors of disease and treatment, patients' personal experience and demographic information were used to construct the nomogram. For patients at high risk of CINV, clinicians should consider modifying the antiemetic regimen. Additional actions that could be taken to prevent CINV include psychological or dietary interventions, or multidisciplinary team management of symptoms such as pain or insomnia, as recommended by National Comprehensive Cancer Network guidelines (Chan et al. 2017). On the other hand, the nomogram was also useful for patients at low risk of CINV as it can reduce the risk of overtreatment.

The nomogram is a statistical model for predicting individual clinical events by quantifying the corresponding risk based on different factors. The nomogram in the present study was established as follows: according to the classification of each variable in the nomogram, the score was obtained for each prediction index and incorporated into the total score; the corresponding predicted risk value represented the probability of CINV occurrence in breast cancer patients after chemotherapy. Based on the multifactor regression results, the regression coefficient was multiplied by 10 and integer values were rounded and assigned to cor-

responding variables, thus establishing the regression equation that was then presented in the form of a nomogram. This prediction model for CINV risk had an accuracy of 0.78 in the training set, as revealed by the C-index. Compared to previous prediction tool, the curve area of the previous model is only 0.69 (Dranitsaris et al. 2017), so the efficiency of our model is higher. Importantly, we validated the nomogram using an independent validation dataset from an observational study of CINV prevalence, which reflects the CINV burden of breast cancer patients in a real-world setting. It ensured this nomogram the clinic applicability. In validation set, the C-index was 0.74 (95% CI, 0.62-0.85), supporting the external validity of the predictive model. Moreover, the external validation performed using an independent dataset (another hospital patient data) makes our results more robust and convincing. It is generally thought that AUC > 0.7 indicates good discriminatory power; our C-index of 0.74 demonstrates the strength or our model, which is further underscored by the sensitivity and specificity values and the consistency between predicted and actual observations in the calibration plot. Thus, the developed nomogram is reliable and has good clinical applicability.

Women have a higher risk of CINV than men (Roila et al. 2017). Our prediction model for CINV is specific to women with breast cancer, and includes the following variables: history of CINV, metastasis, symptom distress, chemotherapy cycle, and chemotherapy regimen. Younger age has been reported as a key predictor of CINV (Shimokawa et al. 2019; Tsuji et al. 2019), but this was not the case in our study. This may be because young patients have better adherence to antiemetic drugs. The results of our analysis also refute the widely held view that antiemetic drugs and anxiety are related to CINV. This may be due to the strong correlation between these and other variables (such as history of CINV); when all variables were evaluated simultaneously, some became less significant for CINV prediction. The same may apply to the other variables examined in our study, including history of motion sickness and performance status (PS), which also failed to consistently predict CINV contrary to the previous evidence (Molassiotis et al. 2013; Hayashi et al. 2018). Although there were some differences, in general the variables included our nomogram were consistent with those in previous studies, including history of CINV (Dranitsaris et al. 2017; Hayashi et al. 2018; Lee et al. 2017). Symptoms of distress mainly include pain and insomnia; pain has been linked to the development of CINV (Molassiotis et al. 2013), which is supported by our data. Our study implied that patients in earlier cycles (cycle no. < 3) are at higher risk of CINV, which is consistent with previous study (Dranitsaris et al. 2009). Patients who have experienced chemotherapy gradually may acclimate to the process and may be able to better withstand the adverse reactions. Chemotherapy regimen was the strongest predictor of CINV in our study; this is in agreement with the finding that HEC regimens are 3-9 times more likely than LEC regimens to cause CINV (National Comprehensive Cancer Network 2020). It is of interest that oncology metastasis was found to be a protective factor because CINV does not typically occur in metastatic cancer patients in our study; the mechanistic basis for this association warrants further study.

Despite the advantages of our prediction nomogram, it had certain shortcomings and requires refinement before it can be used in clinical practice. Our study was limited by a small sample size; the model needs to be validated in a larger cohort, which could also reveal additional predictive variables for inclusion in the model. Furthermore, as our cohort included only Chinese subjects, the model may not be generalizable to other populations; there is some evidence that emetic susceptibility is higher among Asian and especially Chinese patients (Hassan and Yusoff 2010; Bourdeanu et al. 2012). Another shortcoming was that the AUC value was not extremely high; the discriminatory power of our nomogram may be strengthened by repeating the analysis using data from a larger cohort.

The nomogram developed in this study could assist clinicians in estimating a patient's risk for CINV and making appropriate decisions regarding the use of antiemetics. This could, in turn, enhance patient care by providing optimal antiemetic therapy to those who would most benefit while avoiding its unnecessary use, thereby reducing costs and undesirable side effects such as constipation.

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Conflict of Interest

The authors declare no conflict of interest.

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