Nomogram for Predicting the Overall Survival and Cancer-Specific Survival of Patients with Occult Breast Cancer: A Population-Based Study

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Abstract

Background: Occult breast cancer is a rare breast tumor, whose prognostic nomogram model has not been established. Thus, we aim to develop and validate a nomogram for evaluating the overall survival (OS) and cancer-specific survival (CSS) of patients with occult breast cancer.

Methods: Between 2004 and 2015, 704 eligible occult breast cancer patients were screened from the Surveillance, Epidemiology, and End Results (SEER) database using specific inclusion and exclusion criteria and then included in the surveillance. They were randomly divided into a training cohort (n = 494) and a validation cohort (N = 210). Univariate and multivariate Cox analyses were performed to explore independent prognostic factors and establish two survival-related nomograms. Area under the curve (AUC), consistency index (C index), internal and external validation calibration curve, decision curve analysis (DCA), Kaplan-Meier analysis, and subgroup analysis were used to evaluate the nomogram.

Results: A total of seven variables were considered to be independent prognostic factors for overall survival (OS) and cancer-specific survival (CSS): age, chemotherapy, radiotherapy, Progesterone receptor (PR) status, N stage, number of lymph node examinations, and number of positive lymph nodes. In the training cohort, the OS nomogram-predicted AUC for three, five, and ten years were 0.792, 0.775, and 0.783, respectively, while those of the CSS nomogram were 0.807, 0.817, and 0.812, respectively. The calibration chart showed excellent agreement between the actual and the nomogram-predicted survival rates in both the training and validation cohorts. The C-index values of the OS nomogram in the training and validation cohorts were 0.762 and 0.782, respectively, while those of the CSS nomogram were 0.786 and 0.816, respectively. DCA and subgroup analysis proved the usefulness of nomograms.

Conclusion: The developed nomogram provided a comprehensive visual model of the risk of each prognostic factor. It can be conveniently used as a personalized prediction tool for the prognosis of occult breast cancer patients.

Full Text

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Tables

Table 1. Patients’ detailed general information (n = 704)

Characteristic	Training Cohort 494)	(n =	Validation Cohort = 210)	(n
	N	%	N	%
Age(years)				
25-54	179	36.2	82	39.0
55-74	261	52.8	105	50.0
>74	54	10.9	23	11.0
Race				
White	386	78.1	175	83.3
Black	65	13.2	24	11.4
Other	40	8.1	11	5.2
Unknown	3	0.6	0	0
Laterality				
Left	245	49.6	103	49.0
Right	208	42.1	88	41.9
Bilateral	1	0.2	2	1.0
Other	40	8.1	17	8.1
Marital status				
Married	266	53.8	129	61.4
Not married b	213	43.1	77	36.7
Other	15	3.0	4	1.9
Grade				
I and II	22	4.5	11	5.2
III and IV	119	24.1	42	20.0
Unknown	353	71.5	157	74.8
Nodal stage				
N1	311	63.0	127	60.5
N2	85	17.2	31	14.8
N3	98	19.8	52	24.8

Estrogen receptor status				
Positive	252	51.0	106	50.5
Negative	193	39.1	83	39.5
Others	49	9.9	21	10.0
Progesterone receptor status				
Positive	168	34.0	66	31.4
Negative	266	53.8	120	57.1
Others	60	12.1	24	11.4
HER-2 status				
Positive	73	14.8	30	14.3
Negative	158	32.0	65	31.0
Others	263	53.2	115	54.8
Surgery				
Lumpectomy	65	13.2	21	10.0
Mastectomy	148	30.0	74	35.2
None	274	55.5	113	53.8
Unknown	7	1.4	2	1.0
Radiation				
Yes	265	53.6	102	48.6
No	229	46.4	108	51.4
Chemotherapy				
Yes	397	80.4	161	76.7
No/Unknown	97	19.6	49	23.3
No. of examined lymph nodes				
0	12	2.4	6	2.9
1-3	72	14.6	28	13.3
4-9	62	12.6	26	12.4
10-	271	54.9	123	58.6
Unknown				

	77	15.6	27	12.9
No. of positive lymph nodes				
0				
1-3	13	2.6	3	1.4
4-9	240	48.6	108	51.4
10-	76	15.4	29	13.8
Unknown	53	10.7	32	15.2
	112	22.7	38	18.1

Table 2. Survival analyses of overall survival for occult breast cancer patients in training cohort

Variables	Univariate	multivariate	
	P	HR(95%CI)	P
Age(years)	<.001		<.001
25-54		Reference	
55-74		1.564(.934-2.620)	.089
>74		3.392 (1.837-6.260)	<.001
Race	.480		
White			
Black			
Other			
Unknown			
Laterality	.069		
Left			
Right			
Bilateral			
Other			
Marital status	.049		.484
Married		Reference	
Not married b		1.186 (.775-1.816)	.432
Other		1.971 (.552-7.035)	.296
Grade	.322		
I and II			
III and IV			
Unknown			
Nodal stage	<.001		.023
N1		Reference	
N2		1.054(.373-2.976)	.921
N3		2.444 (1.235-4.839)	.010
Estrogen receptor status	<.001		.210

Positive		0.660 (0.381-1.143)	.138
Negative		Reference	
Others		2.434 (0.300-19.772)	.405
Progesterone receptor status	.002		.008
Positive		0.359 (0.182-0.709)	.003
Negative		Reference	
Others		0.295 (.039-2.239)	.238
HER-2 status	.248		
Positive			
Negative			
Others			
Surgery	.234		
Lumpectomy			
Mastectomy			
None			
Unknown			
Radiation	.003		.007
Yes		0.525 (0.327-0.841)	.007
No		Reference	
Chemotherapy	<.001		.009
Yes		0.519(0.318-0.848)	.009
No/Unknown		Reference	
No. of examined lymph nodes	<.001		.018
0			
1-3		Reference	
4-9		2.709(0.649-11.307)	.172
10-		1.276(0.260-6.269)	.764
Unknown		0.760 (0.185-3.116)	.703
		0.947(0.332-2.702)	.918
No. of positive lymph nodes	<.001		.090

0		
1-3	Reference	
4-9	2319.823(0-7.402e+40)	.860
10-	8129.127(0-2.601e+41)	.838
Unknown	6231.362(0-1.990e+41)	.843
	7272.320(0-2.329e+41)	.840

Table 3. Survival analyses of cancer-specific survival for occult breast cancer patients in training cohort

Variables	Univariate	multivariate	
	P	HR(95%CI)	P
Age(years)	<.001		.021
25-54		Reference	
55-74		1.194(0.680-2.097)	.537
>74		2.519 (1.260-5.037)	.009
Race	.400		
White			
Black			
Other			
Unknown			
Laterality	.093		
Left			
Right			
Bilateral			
Other			
Marital status	.092		
Married			
Not married b			
Other			
Grade	.356		
I and II			
III and IV			
Unknown			
Nodal stage	<.001		.010
N1		Reference	
N2		1.589(0.477-5.290)	.451
N3		3.118 (1.490-6.522)	.003
Estrogen receptor status	<.001		.263

Positive		0.572 (0.291-1.122)	.104
Negative		Reference	
Others		4.206e+03(0-3.401e+44)	.862
Progesterone receptor status	.008		.263
Positive		0.428 (0.193-0.951)	.104
Negative		Reference	
Others		0 (0-1.616e+39)	.862
HER-2 status	.404		
Positive			
Negative			
Others			
Surgery	.267		
Lumpectomy			
Mastectomy			
None			
Unknown			
Radiation	.013		.004
Yes		0.445 (0.256-0.773)	.004
No		Reference	
Chemotherapy	.009		.140
Yes		0.642(0.356-1.157)	.140
No/Unknown		Reference	
No. of examined lymph nodes	<.001		.006
0		Reference	
1-3		2.994(0.600-14.926)	.181
4-9		2.177(0.383-12.363)	.380
10-		0.505(0.100-2.548)	.408
Unknown		1.152(0.381-3.482)	.802
No. of positive lymph nodes	<.001		.026
0		Reference	

1-3	2.246e+03(0-3.193e+48)	.884
4-9	8.235e+03(0-1.175e+49)	.865
10-	1.395e+04(0-1.985e+49)	.857
Unknown	9.836e+03(0-1.403e+49)	.862

Figures

Figure 1

Nomogram predicting overall survival (OS) of occult breast cancer patients

Figure 2

Nomogram predicting cancer-specific survival (CSS) of occult breast cancer patients

Figure 3

Performance of nomogram via receiver operating characteristic (ROC) curve

Figure 4

Internal and external calibration nomogram for overall survival (OS)

Figure 5

Internal and external calibration nomogram for cancer-specific survival (CSS)

Figure 6

Decision curve analysis of the training cohort (A, C, E) and validation cohort (B, D, F) for 3403-, 5-, and 10-years overall survival (OS) to compare the net benefit of the nomogram and the AJCC 341 stage.

Figure 7

Decision curve analysis of the training cohort (A, C, E) and validation cohort (B, D, F) for 3443-, 5-, and 10-years cancer-specific survival (CSS) to compare the net benefit of the nomogram and 345the AJCC staging.

Figure 8

Survival analysis of patients after risk-stratification (A and B for overall survival (OS); C 348 and D for cancer-specific survival (CSS)).