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ORIGINAL RESEARCH

Prognostic Values Of Preoperative Serum CEA And CA125 Levels And Nomograms For Young Breast Cancer Patients

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Background: Young breast cancer patients have poor prognosis compared to older patients in both overall survival (OS) and loco-regional failure-free survival. Carcinoembryonic antigen (CEA) and Cancer antigen 125 (CA125) have been widely used, but their prognostic value in young breast cancer patients remains unknown. The objectives of this study were to evaluate the prognostic value of preoperative CEA and CA125 serum levels and to build nomograms for better prognostic prediction of young Chinese breast cancer patients using both tumor markers.

Methods: We included 576 young breast cancer patients (≤40 years at diagnosis) and collected their preoperative information. The best cut-off values of the CEA and CA125 were identified with receiver operating characteristic (ROC) curves. Univariate and multivariate analyses were used to identify the relative risks of factors for the overall survival (OS), and disease-free survival (DFS), and nomograms were constructed based on these identified factors.

Results: The best cut-off values for CEA and CA125 in young breast cancer patients was 3.38 ng/mL and 19.38 U/mL, respectively. Kaplan-Meier analysis showed that young patients with low levels of CEA and/or CA125, had longer OS and DFS. Multivariate analysis suggested that both CEA and CA125 levels were independent predictive elements for OS. Nomograms were built and showed a better predictive ability for OS (AUC = 0.856) and DFS (AUC = 0.702) in young breast cancer patients.

Conclusion: Preoperative serum CEA and CA125 levels could be the independent prognostic factors for OS, and the nomograms including these two variables provide more personal forecasts information to help physicians optimize treatment for young breast cancer patients better.

Keywords: young breast cancer patient, carcinoembryonic antigen, cancer antigen 125, prognostic factors

Introduction

Breast cancer is the most commonly occurring female cancer in worldwide, and its incidence and mortality rates are expected to increase significantly in the next decade. Most breast cancers are diagnosed in patients who are 50 and older, but its breast cancer also affects younger women, approximately 6–7% of breast cancer patients are ≤40 years.[1] These young breast cancer patients are more likely to experience malignant biological behaviors and more aggressive phenotypes (larger tumor size, hormone receptor-negative, advanced pathologic grade, and more lymph node metastasis).[2–5]

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For young breast cancer patients, there is no significant long-term prognosis difference between breast-conserving surgery plus radiation and modified radical mastectomy in the long term prognosis.[6,7] Young breast cancer patients also have poorer prognosis than older patients with regard to both in overall survival (OS) and loco-regional failure-free survival.[8,9] Therefore, better monitoring methods, such as mammography and magnetic resonance imaging (MRI), are recommended for young patients with breast cancer.[10]

It is a challenge to predict the prognosis of young breast cancer patients and select the optimal treatments. Convenient tumor markers with good predictive ability have recently drawn attention.[11,12] The most recognized breast cancer markers are estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER-2), and Ki-67. These markers can be used to classify patients into different molecular subtypes, and these subtypes are the primary indicators of prognosis in breast cancer.[13–15] Serum tumor markers like carcinoembryonic antigen (CEA) and cancer antigen 153 (CA15-3) in breast cancer have been approved by the US Food and Drug Administration (FDA) for breast cancer tumor monitoring.[16,17] Cancer antigen 125 (CA125) is commonly used to monitor the epithelial ovarian cancer, but relevant reports of CA125 in breast cancer are lacking.[18–21] Recent studies confirmed that the combination of CEA and CA125 could predict prognosis in gastric cancer, lung cancer, pancreatic cancer, and ovarian cancer, but its utility has not been shown for breast cancer.[22–26] In this study, we aim to investigate the prognostic values of preoperative CEA and CA125 serum levels, and to use these markers to build nomograms to better predict prognosis in young patients with breast cancer.

Materials And Methods

Patients And Methods

The retrospective analysis was performed in 576 female patients, who were not older than 40 years, when they were diagnosed with invasive breast cancer. All patients underwent either modified radical mastectomy or breast-conserving surgery between January 2008 and December 2012 at the Sun Yat-sen University Cancer Center (SYSUCC) in China. We collected data from all the invasive breast cancer patients (age ≤ 40 years old) treated during that time period. The SYSUCC ethics boards granted ethical approval, and all patients provided written informed consent. The exclusion criteria were as follows: (1) patients without follow-up; (2) CEA, CA125, or other necessary data could not be extracted; (3) received neoadjuvant chemotherapy before surgery; (4) metastasis at the time of diagnosis; (5) had previous or coexisting cancers; (6) had the severe disease that influence patients' survival.

Clinical Data Collection

Both baseline characteristics and follow-up treatments were included in this study. We detected the serum CEA and CA125 before surgery as routine clinical evaluation factors. Tumor size, lymph nodes, and TNM stage classification were determined according to the American Joint Committee on Cancer 7th edition criteria. Tumor ER and PR positivity corresponded to ≥ 10% nuclear-stained tumor cells. HER-2/neu immunohistochemical staining was scored from 0 to 3+, 3+ was considered positive, and 0 or 1+ were considered negative. Fluorescence in situ hybridization (FISH) tests were performed for patients with HER-2 scored as 2+. Cancer subtypes were classified as luminal A subtype, luminal B subtype, triple-negative subtype, or HER-2 overexpressing subtype according to ER, PR, HER-2, and Ki-67 status. Patients were followed-up by telephone or e-mail by the Department of Follow-up and also submitted to physical examinations and laboratory and radiological imaging tests as needed.

Statistical Analyses

Numbers and percentages are used to describe categorical data. Patients' characteristics' relationships with CEA and CA125 were evaluated by Student's *t*-test or one-way analysis of variance (ANOVA), and differences between variables were examined with Chi-squared tests. Survival analysis was performed with the Kaplan Meier method and log rank testing. One endpoint used in this study was overall survival (OS), and is calculated from the date of diagnosis to death, or last follow-up. The second endpoint was disease-free survival (DFS), it was estimated from the date of diagnosis to recurrence, metastasis, or death. Independent factors in OS and DFS were confirmed using univariate and multivariate analyses. Relative risks of factors were estimated by hazard ratios (HRs) and the corresponding 95% confidence intervals (CIs) from the Cox analysis. Nomograms were established according to the results of multivariate analysis results. The effects of diagnosis of CE and CA125 were determined by area under the curve (AUC) of receiver operating characteristic ROC curve analyses, and their best cut-off values were calculated using the highest Youden's index. The prognostic ability of nomograms was determined by Harrell's

concordance index (C-index), as well as the AUC of the ROC (AUROC). The consistency of nomograms for 5-year OS and DFS were shown in calibration curves. A value of $p < 0.1$ was considered significant in univariate analysis, while $p < 0.05$ was significant for other analyses. The statistical analyses were used SPSS for Windows version 20.0 (IBM Corp., Armonk, NY USA) and R 3.3.3 (http://www.R-project.org) software programs.

Results

Patient Characteristics

In total, 576 young patients with pathologically confirmed as invasive breast cancer treated at SYSUCC from January 2008 to December 2012 were enrolled after careful screening. Among them, 102 (17.7%) patients had developed recurrence, metastasis, or death at the end of the study, 33 (5.7%) patients had died. The median age of these patients was 35.8 years (range: 20 to 40 years), and their median follow-up time was 55 months (range: 3–101 months). The patients' clinicopathological characteristics are shown in Table 1. Overall, 206 (35.8%), 247 (42.9%), and 123 (21.3%) patients were in stages I, II, and III, respectively. The luminal A subtype group had 114 (19.8%) patients, the luminal B subtype had 290 (50.3%) patients, the triple-negative subtype group had 77 (13.4%) patients, and the Her-2 overexpressing group had 67 (11.6%) patients. The subtype was uncertain in 28 (4.9%) patients (Table 1).

ROC Analysis And Optimal CEA And CA125 Cut-Offs

We performed ROC curve analysis and used OS as the endpoint to identify the optimal cut-off values of preoperative serum CEA and CA125. The AUROC curve was 0.710 (95% CI, 0.603–0.818 $p < 0.001$) for CEA and 0.634 (95% CI, 0.528–0.740 p=0.01) for CA125 (Figure 1A). Using the highest Youden's index values, the cut-off points for CEA and CA125 was 3.38 ng/mL and 19.38 U/mL, respectively. We then divided patients into low and high groups according to the CEA or CA125 levels for further study. For CEA, 507 (88.0%) and 69 (12.0%) patients were in the low and high groups, respectively. The corresponding numbers for the low and high CA125 groups were 373 (64.8%) and 203 (35.2%) patients.

The low and high CEA groups showed differences in tumor size, lymph node status, and Her-2 status (all p<0.05). The low and high CA125 groups had significant differences in TNM stage, hormone receptor (ER and PR) status, breast cancer molecular type, and endocrine therapy use (all p<0.05). These results indicate that CEA and CA125 levels reflect different aspects of young breast cancer.

Survival And Prognostic Values Of CEA And/Or CA125 Levels

Kaplan–Meier survival analysis was used to analyze the association of CEA and CA125 levels with OS and DFS in young breast cancer patients. The high CEA group had shorter DFS and OS than low CEA patients (p<0.001 for DFS; p<0.001 for OS Figure 2A and B). As expected, low CA125 group patients had significantly longer DFS and OS than high CA125 group patients (p=0.04 and p<0.001, respectively; Figure 2C and D).

Based on the above analyses, further univariate and multivariate Cox proportional hazard regression analyses were conducted. Variables with p<0.1 in the univariate analysis were entered into the multivariate analysis. Age (≤35 years vs 35<age≤40 years), surgical method, tumor size, lymph node status, ER, CEA, and CA125 had statistical differences for OS in the univariate analysis. In the multivariate analysis, five factors remained statistically significant: young age, more lymph node metastasis, ER negative, high CEA, and high CA125. Using the same methods for DFS, the results showed that age, tumor size, lymph node metastasis, and high CEA were independent prognosis factors. CA125 was not an independent prognosis factor for DFS in young breast cancer (Table 2).

Formulation And Verification Of Nomograms Of Young Breast Cancer Patients

To better evaluate the OS and DFS of young breast cancer patients, nomograms were built based on independent prognostic factors for OS in the multivariate Cox regression model. We labeled the selected factors as age ≤35 years, 0; 35<age≤40 years, 1; lymph node,0 to 3 according to standard TNM stage; ER-positive and -negative as 0 and 1, respectively; and low and high CEA and CA125 as 0 and 1, respectively. The summed scores of each parameter from the nomogram yield the corresponding survival probabilities (e.g., 3-year survival, 5-year survival, and 8-year survival) (Figure 3A and B). The C-index values for OS and DFS were 0.853 (95% CI: 0.789–0.917 (Figure 1C) and 0.699 (95% CI: 0.644–0.754 Figure 1D), respectively. When ROC curve analysis was performed to assess

Table 1 Correlation Between Pre-Therapeutic CEA And CA125 Levels And Variables

Characteristics And Classification		CEA		*p*	CA125		*p*
		Low	High		Low	High	
Age	≤35 >35 and ≤40	192 (87.7) 315 (88.2)	27 (12.3) 42 (11.8)	0.895	134 (61.2) 239(66.9)	85 (38.8) 118 (33.1)	0.178
Surgical method	Yes No	398 (86.7) 109 (93.2)	61 (13.3) 8 (6.8)	0.057	295 (64.3) 78 (66.7)	164 (35.7) 39 (33.3)	0.666
Tumor size	T1 T2 T3 T4	264 (90.7) 222 (88.1) 11 (61.1) 10 (66.7)	27 (9.3) 30 (11.9) 7 (38.9) 5 (33.3)	<0.001*	203 (69.8) 150 (59.5) 12 (66.7) 8 (53.3)	88 (30.2) 102 (40.5) 6 (33.3) 7 (46.7)	0.069
Lymph node status	N0 N1 N2 N3	285 (91.6) 123 (83.7) 60 (89.6) 39 (76.5)	26 (8.4) 24 (16.3) 7 (10.4) 12 (23.5)	0.004*	215 (69.1) 88 (59.9) 41 (61.2) 29 (56.9)	96 (30.9) 59 (40.1) 26 (38.8) 22 (43.1)	0.116
TNM Stage	I II III	187 (90.8) 217 (87.9) 103 (83.7)	19 (9.2) 30 (12.1) 20 (16.3)	0.163	148 (71.8) 151 (61.1) 74 (60.2)	58 (28.2) 96 (38.9) 49 (39.8)	0.029*
ER	Positive Negative	357 (88.6) 150 (86.7)	46 (11.4) 23 (13.3)	0.576	277 (68.7) 96 (55.5)	126 (31.3) 77 (44.5)	0.003*
PR	Positive Negative	347 (87.8) 160 (88.4)	48 (12.2) 21 (11.6)	0.891	271 (68.6) 102 (56.4)	124 (31.4) 79 (43.6)	0.005*
HER2	Positive Negative Miss	146 (83.0) 352 (90.7) 9 (75.0)	30 (17.0) 36 (9.3) 3 (25.0)	0.012*	119 (67.6) 243 (62.6) 11 (91.7)	57 (32.4) 145 (37.4) 1 (8.3)	0.074
Types	Miss Luminal A Luminal B Triple negative Her-2 overexpress	24 (85.7) 107 (93.9) 249 (85.9) 71 (92.2) 56 (83.6)	4 (14.3) 7 (6.1) 41 (14.1) 6 (7.8) 11 (16.4)	0.106	21 (75.0) 79 (69.3) 196 (67.6) 36 (46.8) 41 (61.2)	7 (25.0) 35 (30.7) 94 (32.4) 41 (53.2) 26 (38.8)	0.006*
Adjuvant chemotherapy	Yes No	461 (87.8) 46 (90.2)	64 (12.2) 5 (9.8)	0.821	334 (63.6) 39 (76.5)	191 (36.4) 12 (23.5)	0.090
Adjuvant radiotherapy	Yes No Miss	178 (90.8) 294 (85.7) 35 (94.6)	18 (9.2) 49 (14.3) 2 (5.4)	0.095	116 (59.2) 233 (67.9) 24 (64.9)	80 (40.8) 110 (32.1) 13 (35.1)	0.124
Endocrine treatment	Yes No Miss	360 (87.0) 102 (90.3) 45 (91.8)	54 (13.0) 11 (9.7) 4 (8.2)	0.436	279 (67.4) 59 (52.2) 35 (71.4)	135 (32.6) 54 (47.8) 14 (28.6)	0.007*

Note: *$p < 0.05$ was considered statistically significant.
Abbreviations: ER, Estrogen receptor; PR, Progesterone receptor; HER-2, Human epidermal growth factor receptor-2; Miss, means data missing.

prognosis ability, the combined AUC was 0.856 (95% CI: 0.793–0.919) for OS; a higher value was observed for CEA (AUC=0.710; 95% CI: 0.603–0.818) than for CA125 (AUC=0.634; 95% CI: 0.528–0.740) (Figure 1A). With regard to DFS, the combined AUC=0.702 (95% CI: 0.645–0.759) was also higher than for individual CEA (AUC=0.615; 95% CI: 0.551–0.679) or CA125 (AUC=0.551; 95% CI: 0.488–0.615) (Figure 1B).

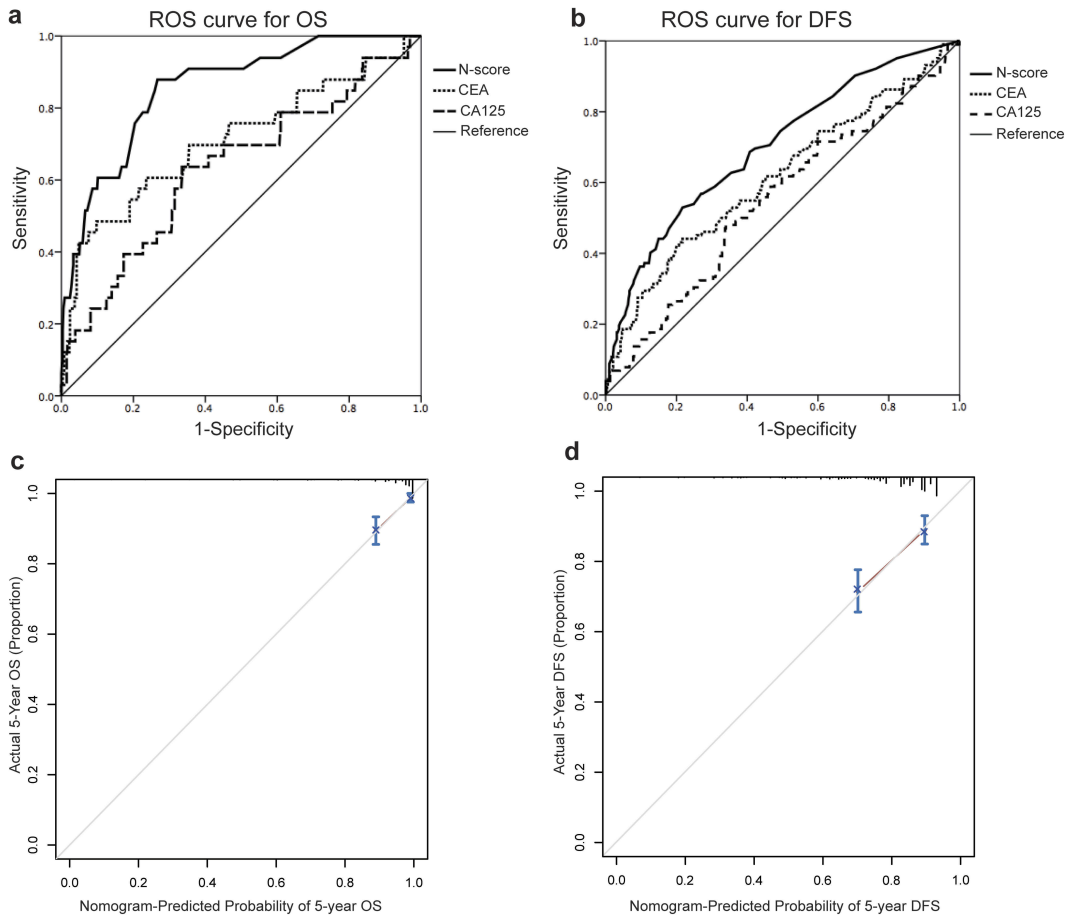

Figure 1 The prognostic values for OS and DFS. (**A**) Prognostic values for nomogram scores, CEA, and CA125 to OS calculated by ROC curves; AUC=0.856, 95% CI: 0.793–0.919) for nomogram; AUC=0.710, 95% CI: 0.603–0.818 for CEA; and AUC=0.634, 95% CI: 0.528–0.740 for CA125; (**B**) Prognostic values for nomogram scores, CEA, and CA125 to DFS calculated by ROC curves; AUC=0.702, 95% CI: 0.645–0.759 for nomogram; AUC=0.615, 95% CI: 0.551–0.679 for CEA; AUC=0.551, 95% CI: 0.488–0.615 for CA125; (**C**) Calibration curve for 5-year OS of the nomogram; (**D**) Calibration curve for 5-year DFS of the nomogram.

Abbreviations: AUC, area under the curve; CA, cancer antigen; CEA, carcinoembryonic antigen; DFS, disease-free survival; OS, overall survival; N-score, nomogram-score; ROC, receiver operating curve.

Risk Group Re-Stratification Based On The Nomograms

Among the 576 young breast cancer patients, standard TNM staging showed no significant statistical differences between stages I and II for OS (p=0.06) and DFS (p=0.215) (Figure 2E and F). Based on the total scores, we divided patients into three risk subgroups for OS (score from OS nomogram: 0–104, group 1; 104–191, group 2; >191, group 3) and DFS (Score from DFS nomogram: 0–60, group 1; 60–143, group 2; and >143, group 3). The re-stratified groups showed statistically significant differences (Figure 4A and B), including remarkable differences in each TNM stage (Figure 4C–H).

Discussion

Breast cancer is the most common cancer in women with the second-highest mortality rate. Age has a strong influence on breast cancer outcomes. Patients younger than 40 have many differences compared to older patients. Breast cancer is the leading cause of cancer death between ages 20 and 39, while it is the second most common cause of cancer death after lung cancer in patients older than 40.[27] The incidence of young breast cancer has continually increased in the Asian population.[28] Young breast cancer patients tend to develop phenotypes that are more malignant leading to more aggressive biologic behavior so more effective diagnostic and prognostic methods should be used in this population.[3,4] Besides intrinsic tumor characteristics such as TNM stage and molecular classification, serum biomarkers have drawn increasing attention for predicting prognosis. In this study, high serum CEA and CA125 were independent negative predictive factors for OS in young breast cancer patients.

CA125 is encoding by the *MUC16* gene and is a prognostic indicator for many cancers, especially in gynecological

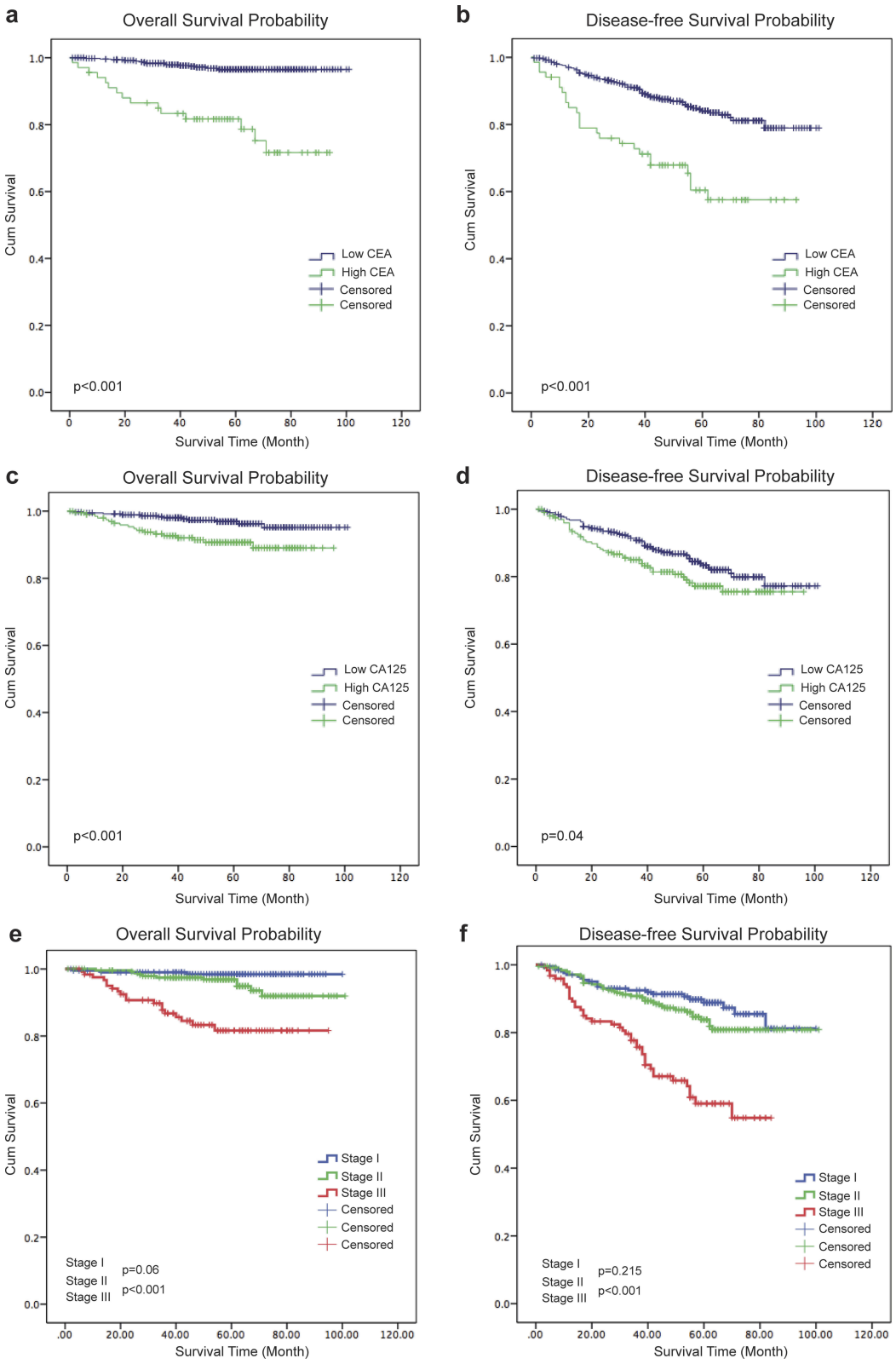

Figure 2 Kaplan-Meier curve estimates of the OS (**A**) and DFS (**B**) of young breast cancer patients. (**A**) The OS rate and (**B**) DFS rate of young breast cancer patients at different CEA levels; (**C**) The OS rate and (**D**) DFS rate of young breast cancer patients at different CA125 levels; (**E**) The OS rate and (**F**) DFS rate of young breast cancer patients at different standard TNM stages.

Abbreviations: CA, cancer antigen; CEA, carcinoembryonic antigen; DFS, disease-free survival; OS, overall survival; TNM, tumor, node, metastasis.

Table 2 Univariate And Multivariate Analyses For OS And DFS In Young Breast Cancer Patients

Variables		Overall Survival (OS)				Disease-Free Survival (DFS)			
		Univariate Analysis		Multivariate Analysis		Univariate Analysis		Multivariate Analysis	
		HR (95% CI)	*p*	HR (95% CI)	*p*	HR (95% CI)	*p*	HR (95% CI)	*p*
Age (35–40 vs ≤35)		0.375 (0.187–0.755)	0.006*	0.324 (0.157–0.670)	0.002*	0.629 (0.426–0.928)	0.019*	0.565 (0.379–0.844)	0.005*
Surgical method (breast conserving surgery vs modified radical mastectomy)		0.263 (0.063–1.101)	0.067*	0.603 (0.135–2.686)	0.507	0.815 (0.484–1.373)	0.590		
Tumor size	T1	1 (reference)		1 (reference)		1 (reference)		1 (reference)	
	T2	2.028 (0.929–4.430)	0.076*	1.060 (0.452–2.488)	0.893	1.083 (0.709–1.654)	0.712	0.675 (0.428–1.064)	0.091
	T3	1.760 (0.225–13.767)	0.590	0.384 (0.043–3.450)	0.393	2.416 (1.029–5.671)	0.043*	0.990 (0.385–2.541)	0.983
	T4	12.956 (4.419–37.991)	< 0.001*	2.616 (0.672–10.186)	0.166	7.741 (3.890–15.403)	< 0.001*	3.047 (1.360–6.829)	0.007*
Lymph node status	N0	1 (reference)		1 (reference)		1 (reference)		1 (reference)	
	N1	3.082 (1.097–8.660)	0.033*	1.743 (0.550–5.519)	0.345	2.710 (1.662–4.420)	< 0.001*	2.613 (1.565–4.364)	< 0.001*
	N2	10.141 (3.745–27.467)	< 0.001*	10.520 (3.453–32.046)	< 0.001*	4.137 (2.336–7.328)	< 0.001*	4.958 (2.673–9.196)	< 0.001*
	N3	8.342 (2.802–24.835)	< 0.001*	4.404 (1.116–17.379)	0.034*	4.480 (2.459–8.161)	< 0.001*	3.253 (1.582–6.688)	0.001*
ER (no vs yes)		2.264 (1.144–4.482)	0.019*	2.790 (1.361–5.720)	0.005*	1.480 (0.990–2.211)	0.056*	1.486 (0.985–2.240)	0.059
PR (no vs yes)		1.732 (0.868–3.455)	0.119			1.370 (0.914–2.052)	0.127		
HER-2 (no vs yes)		0.735 (0.361–1.495)	0.395			0.830 (0.549–1.254)	0.376		
CEA (high vs low)		7.215 (3.643–14.289)	< 0.001*	7.517 (3.504–16.124)	< 0.001*	2.785 (1.784–4.348)	< 0.001*	2.345 (1.459–3.769)	< 0.001*
CA125 (high vs low)		3.409 (1.677–6.928)	0.001*	2.509 (1.205–5.223)	0.014*	1.503 (1.016–2.224)	0.042*	1.346 (0.902–2.008)	0.146

Notes: *$p < 0.1$ was considered statistically significant in Univariate analysis. $p < 0.05$ was considered statistically significant in Multivariate analysis.

Abbreviations: OS, overall survival; DFS, Disease-free survival; HR, hazard ratio; CI, confidence interval; ER, Estrogen receptor; PR, Progesterone receptor; HER-2, Human epidermal growth factor receptor-2.

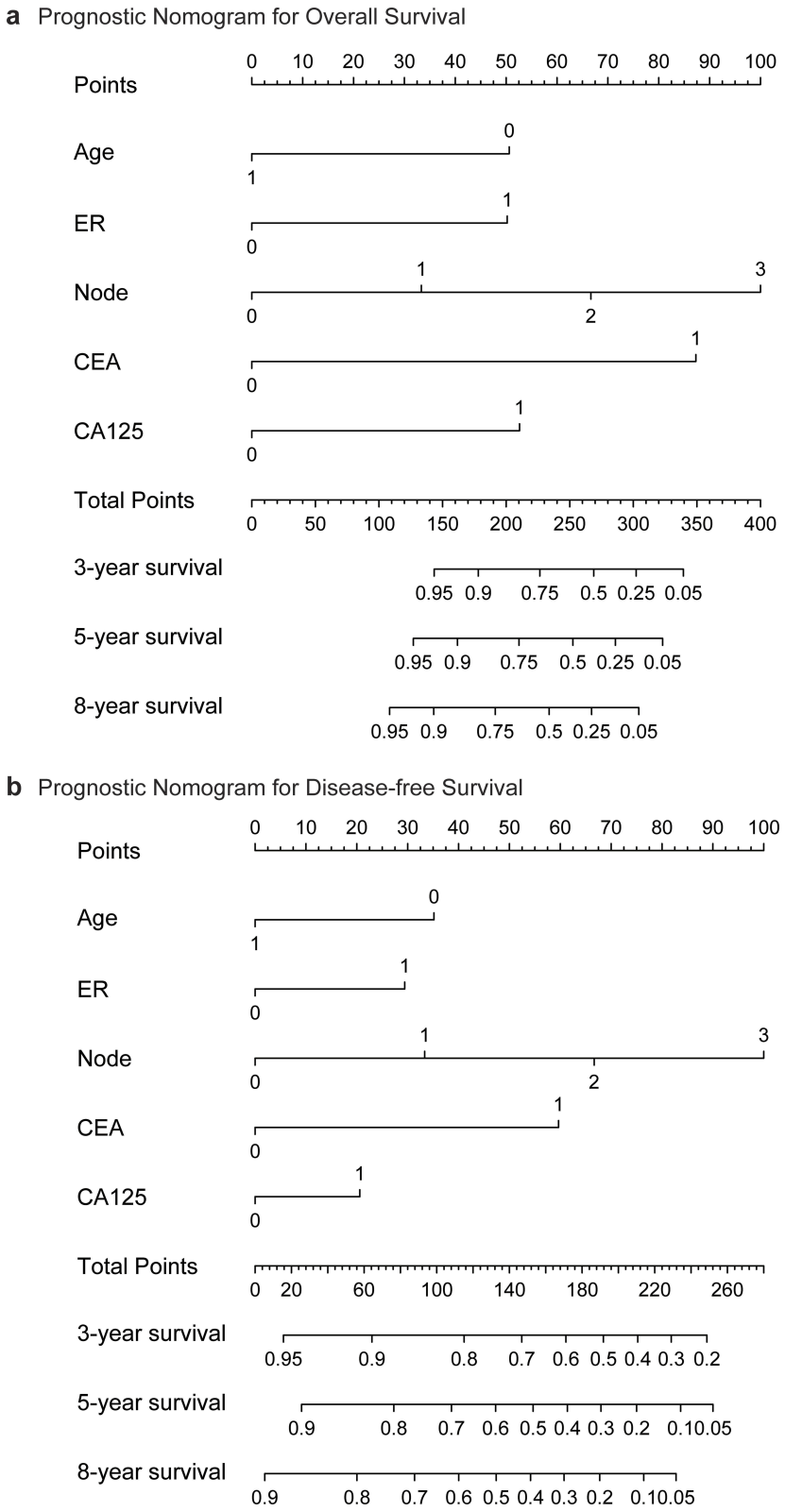

Figure 3 Established nomograms. (**A**) Nomograms predict the OS and (**B**) DFS of young breast cancer patients via the clinicopathological characteristics and pretreatment serum cancer biomarkers.
Abbreviations: DFS, disease-free survival; OS, overall survival.

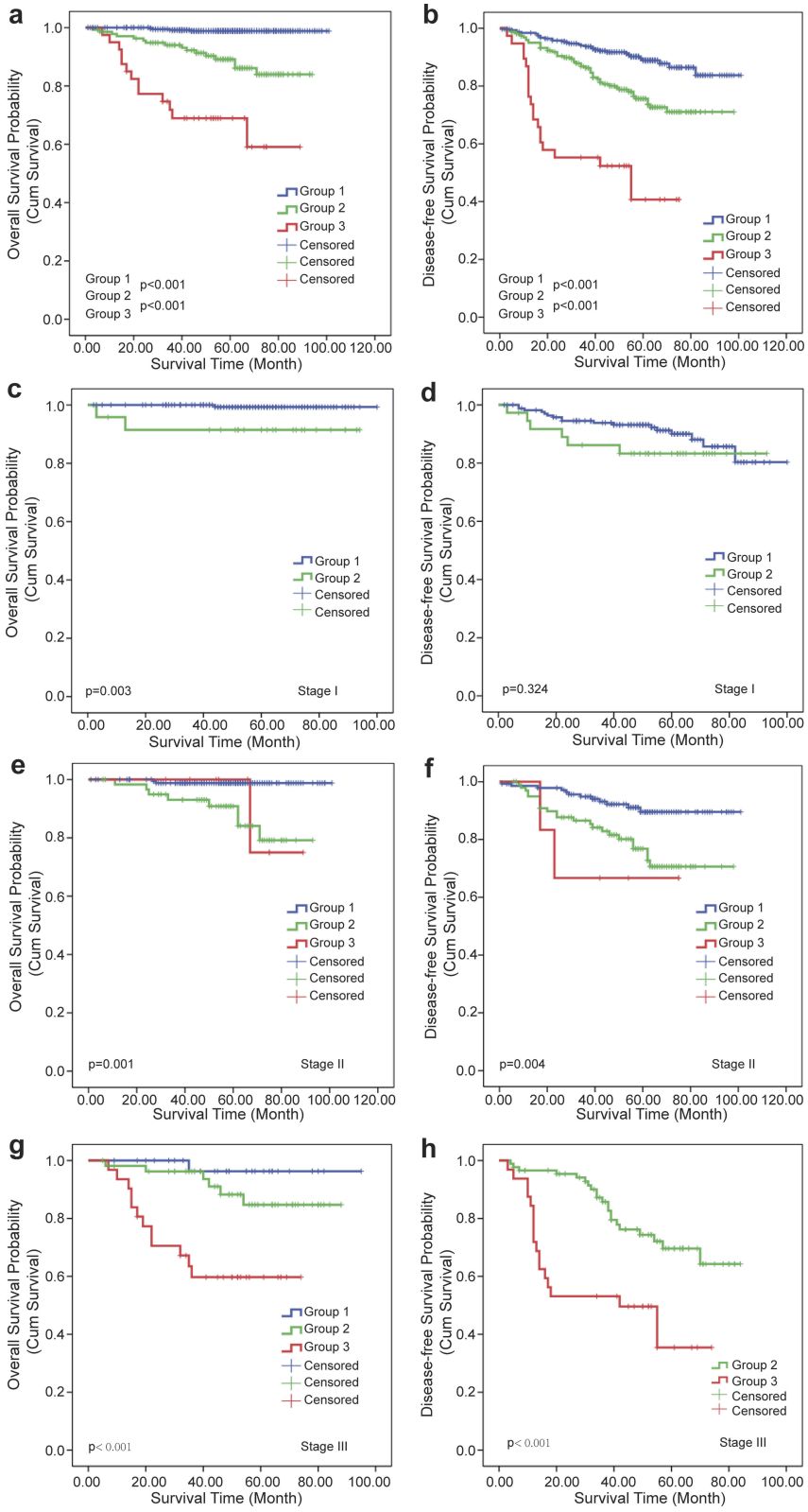

Figure 4 Risk group stratification analysis at each TNM stage. (**A**) The OS and (**B**) DFS of all patients in each score group. (**C, E, G**) The OS and (**D, F, H**) DFS of patients at TNM stage I, II, and III, respectively.

Abbreviations: DFS, disease-free survival; OS, overall survival; TNM, tumor, node, metastasis.

oncology,[29–31] but the precise effect of CA125 on breast cancer remains ambiguous. Several studies reported that CA125 is not suitable for diagnosing and grading breast cancer patients and may even be redundant if other biomarkers such as CA15-3 are used.[21,32,33] There are no published data regarding the predictive value of CA125 in breast cancer; however, CA125 has been associated with metastasis in this population. Specifically, patients with higher CA125 levels were more likely to experience metastasis to the pleura or nearby costal bone and lung.[34,35] Even though higher CA125 did not have predictive value in all breast cancer patients; it has been associated with prognosis in patients with recurrent or stage IV breast cancer.[20,34] Elevated CA125 in breast cancer may be related to future gynecological oncology development.[19,36] In our retrospective study, CA125 in young breast cancer patients had a good predictive value on ROC curve analysis, and the optimal cut-off value was 19.38 U/mL. CA125 also showed a correlation with ER and PR status, which is in accordance with previous ovarian cancer studies.[37,38] This may be related to cell adhesion and should be elucidated in future studies. Kaplan-Meier survival analysis showed longer OS and DFS in the low CA125 group, while multivariate analysis suggested that CA125 was an independent prognostic factor for OS but not DFS in young breast cancer patients.

CEA is a widely used tumor marker for examination and prediction in many cancers.[39–42] In our study, the best CEA cut-off value in young breast cancer patients was 3.38 ng/mL, and the low and high groups exhibited differences in tumor size, lymph node metastasis, and HER-2 status. A previous study reported that higher CEA was significantly more common in HER-2 positive patients,[43] and this result complements the results of CA125, suggesting that combining CEA and CA125 may be a comprehensive marker for young patients with breast cancer. Higher serum CEA was associated with shorter OS and DFS, and in univariate and multivariate analyses, CEA was an independent negative predictive factor for both OS and DFS in young breast cancer patients.

A single tumor marker is not sufficient for predicting cancer prognosis. Many studies focused on the use of multiple markers to increase prognostic accuracy.[44] One group combined different tumor markers for breast cancer diagnosis and prognosis,[45] while another used other biomarkers to supplement tumor markers' predictive abilities.[46] We previously developed a nomogram system that combined histological tumor grade, lymph node stage, and CEA and CA15-3 levels in triple-negative breast cancer that showed useful utility.[47] Intrinsic tumor characteristics such as tumor burden and hormone receptor status are strongly associated with breast cancer prognosis. To obtain better predictive ability for young breast cancer patients that helps physicians develop optimal therapeutic schedules, we integrated intrinsic tumor biomarkers and the serum tumor markers CEA and CA125 in easy-to-use nomograms. This convenient assessment method gives each patient a personalized prognostic prediction, which can help doctors choose more suitable treatments and monitoring methods.

Conclusion

In summary, this study is the first to investigate the use of tumor markers for the prognostic assessment of young breast cancer patients. We found that both CEA and CA125 could be independent prognostic factors of OS for this population. Considering preoperative serum levels of CEA and CA125 in combination with other useful molecular factors; we built novel nomograms to better predict the OS and DFS of these patients. These nomograms can help doctors more effectively predict the prognosis of young breast cancer patients, and they can be used as references to select appropriate adjust follow-up treatments.

Abbreviations

AUC, area under the curve; CA, cancer antigen; CEA, carcinoembryonic antigen; DFS, disease-free survival; OS, overall survival; N-score, nomogram-score; ROC, receiver operating curve; TNM, tumor, node, metastasis.

Ethical Approval

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 Declaration of Helsinki and its later amendments or comparable ethical standards.

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Disclosure

The authors declare that there are no conflicts of interest in this work.

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