A Lymph Node Classification-based cancer-specific Survival Predicting Model in Patients with Ampullary cancer: A Derivation and Validation Study

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Research

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Abstract

Background: Current lymph node (LN) staging is controversial in predicting the survival of ampullary cancer (AC). We aimed to develop an alternative LN-classification-based nomogram to individualize AC prognosis.

Methods: Using the data of patients diagnosed with AC between 2004 and 2015 from the SEER database, we determined the cut-off values for the number of LNs examined via the K-adaptive partitioning algorithm. A nomogram predicting the survival of AC patients was performed, internally and externally validated, and evaluated by calibration plot, C-index, and decision curve analysis (DCA), and was compared to the 7th TNM stage.

Results: We included 2341 patients with detailed information. The optimal cut-off for examined LN number was 12, while the cut-off value for positive LNs was 0 and 4. The C-index for the nomogram was higher than that of the 7th TNM staging (internal: 0.686; 95% CI, 0.584-0.773 vs. 0.616; 95% CI, 0.533-0.754, P < 0.001; external: 0.713; 95% CI, 0.651-0.784 vs. 0.647; 95% CI, 0.551-0.719, P < 0.001). Additionally, the nomogram showed good agreement between internal and external validation. DCA analysis showed no matter in the internal cohort or external cohort; the nomogram showed a greater benefit across the period of follow-up than did the 7th TNM stage.

Conclusion: We found that examined LNs that were more than 12 were beneficial for prognosis of patients. We also modified the current N staging into three groups based on number of metastatic LNs: N0, no LN metastasis; N1, 1–4 metastatic LNs; N2, >=5 metastatic LNs. A nomogram with greater benefit for predicting the survival of patients with AC than TNM staging was constructed.

1 Introduction

Ampullary cancer (AC) which accounts for 0.2% of all gastrointestinal tumors is a rare malignant tumor derived from the ampulla of vater[1]. According to an earlier report, the incidence was about one per 100 000, whereas the newly diagnosed cases have obviously increased in the recent years based on data from the surveillance, epidemiology, and end results (SEER)[1,2]. Compared to pancreatic tumors, AC has a better survival rate, with a 5-year survival rate of 30–60%[3]. Several studies have demonstrated that some clinicopathological factors such as histology, tumor size and lymph node metastasis (LNM) are associated with the survival of patients with AC[1,3,4]. With respect to histology, for instance, patients with the pancreatobiliary subtype have a poorer 5-year survival rate than those with the intestinal type (27.5% vs. 61%), while patients with the mixed type almost have an intermediate survival rate1,3. Of these factors, lymph node (LN) involvement has been taken as a well-demonstrated factor correlated with the prognosis of patients with AC[5]. However, there are some controversial issues about the number of examined LNs and the category of positive LNs. Nassour et al stated that at least 17 LNs should be examined for optimal LN staging[6], while J. Kwon thought it was of great benefit when the total number of LNs was up to 12[7]. Other studies also found that the number of LNs ranged from 12 to 16[8,9,10]. In

addition, the category of positive LNs was also different among the suggestions proposed by several studies. Kang et al found that metastatic LNs were divided into three groups, namely 0, 1–2 and ≥ 3 positive LNs[8], while Sakata J considered that the cut-off value of positive LNs was 0 and 3[10]. The 7th edition of the AJCC cancer staging suggested that metastatic LNs staging was categorized as absent and present[11]. Also, some studies suggested that the LN ratio was a good predictive factor and the value was 0.15–0.23[5,8,12]. Previous studies have demonstrated that patients with node-positive, pancreatobiliary type had a 5-year survival rate of 20%, while node-negative patients had a better prognosis with a 5-year survival of 47%[13]. Based on these, we aimed to determine the optimal number of examined LNs and an alternative staging of the number of metastasis LNs by a large population-based study.

In our study, the best cut-off points were determined using the K-adaptive partitioning (KAPS) algorithm which was demonstrated as a useful tool to obtain heterogeneous subgroups by survival[14]. Through the SEER database, we developed and validated a nomogram to predict the survival of patients with AC.

2 Methods

2.1 Patients

The data of all patients with AC were retrieved from the SEER database with the National Cancer Institute's SEER*Stat software (version 8.3.6). Informed consent was not required because the SEER database is free for public use. According to the International Classification of Diseases in Oncology (ICD-O-3), tumors with codes C24.1 were identified as AC. In our study, patients with AC were included according to the following criteria: (1) patients older than 20 years who were diagnosed as having AC by positive histology from 2004 through 2015; (2) patients with a detailed record on cancer-specific survival; (3) patients who were recorded with T stage, N stage, and M stage information; and (4) patients with detailed information, including race, grade, examined LNs, tumor size, and positive LNs.

2.2 Clinicopathological factors

The clinicopathological variables extracted from the SEER database in our study included age, race, sex, pathology grade, LNM, M stage, tumor size, T stage, N stage, examined LNs, and positive LNs. The patients were divided into three age groups: < 50 years, 50–70 years, and ≥ 70 years. Race was classified into three types: white, black, and other. Sex included male and female. Pathology grade was categorized as the well/moderately differentiated type and poorly differentiated/undifferentiated type. LNM was described as N1 (Yes) or N0 (No). M1 (Yes) indicated a positive M stage. Tumor size was categorized into four groups: ≤ 2 cm, ≤ 3 cm, ≤ 5 cm, and > 5 cm. With respect to the examined nodes count, according to the results of the KAPS algorithm[14], the cut-off was 12. Therefore, regional nodes examined were divided into two groups: ≤ 12 and > 12. While the cut-off value of positive LNs was 0 and 4, it was divided into three groups: 0, 1–4, and ≥ 5. As for the KAPS algorithm, Soo-Heang Eo et al[15]. Proposed the use of a multi-way split in order to afford an optimal set of cut-off points: the optimal number of groups (K) was

found by a resampling technique which was implemented into an R package that we called KAPS. Simply, the code was available in the previous paper (kaps (formula, data, K = 2:4, mindat, type = c("perm", "NULL"), ...)). In our study, the main observation indicators were cancer-specific survival (CSS). CSS was defined as death attributable to this cancer.

2.3 Statistical analysis

For basic statistical analysis, patients were divided into two groups: the internal cohort included patients diagnosed with EC between 2004 and 2009, while the external validation cohort included those diagnosed between 2010 and 2015. Pearson's chi-squared test was used to investigate the associations between the categorical variables. To explore the potential risk factors for examined LNs, we performed univariate and multivariate logical regression, and we present the results as the odds ratio (OR) with the 95% confidence interval (CI). With respect to CSS of patients who were separated by examined LNs and positive LNs, we performed survival curves using the survminer package in R software. Furthermore, to analyze the related risk factors for survival, we performed multivariate Cox regression, and we determined the variables to perform nomograms according to Akaike Information Criterion (AIC). Finally, we selected CSS as the outcome of interest and performed nomogram based on the multivariate regression analysis. In addition, ROC curve, Calibration plot and DCA were used to assess the validity of the nomogram we constructed. All statistical analyses were performed with the R software (version 3.6.1, StataCorp LLC, College Station, Texas). The main packages used in our study included ggplot2, survival, rms, kaps, and survminer package. The chi-squared test was performed using SPSS (version 24.0). The results were considered to be statistically significant when the P value < 0.05.

3 Results

3.1 Patients Characteristics

As depicted by Supplementary Fig. 1, we enrolled 4990 patients for further investigation; of these, 2341 patients were died due to CSS, and 773 patients died due to other causes. In our evaluations, we considered CSS as the main outcome measure, and hence, we determined 2341 patients to explore prognostic factors. Detailed information of the selected patients is shown in the Table 1. As shown in the Table 1, we found that the age at diagnosis ranged from 50 to 70 years, and black people accounted for the lowest proportion of patients compared to white people (6.84% vs. 77.93%). Interestingly, the pathology grade of AC was superior to moderately and poorly differentiated grades, while the rate of LNM reached 50%. In addition, the tumor size tended to be smaller (≤ 5 cm vs. > 5 cm, 92.95% vs. 7.05%), whereas AC was diagnosed at advanced stages (85.7% vs. 14.3%). In the subgroups divided by years, we found that the examined LNs and T stage were significantly different between the two groups.

3.2 Grouping of LNs in Patients with AC

We applied the KAPS algorithm to determine the categories of examined LNs and positive LNs. The cut-off value of examined LNs was 12, while the values of positive LNs were 0 and 4 (Table 1). As illustrated

by Fig. 1, the Kaplan-Meier survival curve was performed according to the examined LNs and showed that there was an obvious difference between the two groups (P = 0.0014, Fig. 1A). Patients with more than 12 examined LNs have better prognosis than those with less than 12 examined LNs. In addition, with respect to the category of positive LNs, we found that patients with 5 positive LNs had a poorer survival than the other two groups (P < 0.0001, Fig. 1B), suggesting that the optimal groups of metastatic LNs were N0 (no positive LN), N1 (1–4 positive LNs) and N2 (≥ 5 positive LNs). To investigate the factors associated with the count of harvested LNs, we performed univariate and multivariate logistic regression analyses (Table 2). The results showed that patients diagnosed from 2010 to 2015 tended to have more examined LNs compared to those who were diagnosed from 2004 to 2009 (P = 0.000). Patients with bigger tumor sizes were associated with more harvested LNs (P = 0.018). As expected, patients with advanced tumors were inclined to have more LNs harvested. In a nutshell, year of diagnosis, tumor size and T stage were identified as independent factors associated with harvested LNs.

3.3 AC Survival Prediction Model

To construct a survival prediction model, we first performed a multivariate Cox regression analysis and then built a nomogram plot. As listed in Table 3, patients with age > 70 years, advanced T stage, distant metastasis, positive LNM and poorly differentiated had a poorer prognosis, while patients with more examined LNs were correlated with better prognosis. As for building the nomogram, the positive LNs factor was not included due to the fact that the value of AIC was obviously larger when it was enrolled in the nomogram. Therefore, we established a nomogram based on other five prognostic factors (Fig. 2). According to the nomogram, we found that T stage contributed the most to the prognosis of patients with AC, followed by M stage, then pathological grade and age, whereas the examined LNs had the least probability of predicting survival. As for the explanation of the nomogram, a straight line can be drawn down at each time point to determine the estimated probability of survival. With respect to each predictor, we could read the points assigned on a 0–10 scale at the top and then add these points. Finally, we read the corresponding predictions of 1-, 3-, and 5-year risks by finding the number on the “Total Points” scale.

3.4 Validation in the internal and external cohort

To investigate the validity of the nomogram, we divided the patients into internal and external cohorts according to year of diagnosis and determined the C-index value. As listed in Table 4, the value of C-index in the internal cohort was 0.686 (95% CI, 0.584–0.773) and the bootstrap corrected value was 0.674, both of which were higher than the value of TNM stage (C-index, 0.616, 95% CI, 0.533–0.754; bootstrap corrected, 0.615), suggesting that the nomogram was more effective for predicting survival than the TNM stage. In line with the results of the external cohort, the nomogram was superior to TNM stage (external cohort, 0.713, 95% CI, 0.651–0.784, bootstrap corrected, 0.698; TNM stage, 0.647, 95% CI, 0.551–0.719, bootstrap corrected, 0.643). We equally found that there was high consistency between actual and predicted values in the nomogram predicting model (Fig. 3). With respect to the specificity and sensitivity of the nomogram, in the internal cohort, we found that the values of area under the curve (AUC) predicting 1-year, 3-year and 5-year survivals by the nomogram were 0.719 (0.634–0.781), 0.788 (0.672–0.833) and 0.782 (0.653–0.858), respectively, while the values of the TNM stage predicting model were 0.596

(0.537–0.702), 0.673 (0.601–0.714) and 0.689 (0.633–0.768), respectively (Table 4). Compared to the TNM stage model, the nomogram was better at predicting the 1-year, 3-year and 5-year prognoses (Fig. 4A-4C). As indicted by the external cohort, the nomogram also performed better than the TNM stage model (1-year AUC: 0.698 vs. 0.658, 3-year AUC: 0.764 vs. 0.717, 5-year AUC: 0.774 vs. 0.677, $P < 0.001$) (Table 4 and Fig. 4D-4F). Furthermore, to compare the clinical usability between the nomogram and TNM stage models, we performed a DCA plot. As illustrated in Fig. 5, regardless of whether in the internal cohort or in the external cohort, the predicting efficiency of the nomogram was better than that of TNM stage for 1-year, 3-year and 5-year survivals.

4 Discussion

To our knowledge, ACs are tumors located at the junction of the distal bile duct, the main pancreatic duct and the duodenum. They are usually classified into pancreaticobiliary, intestinal and mixed tumors, by which some clinicopathological scores and nomograms have been established to evaluate prognosis[3,16,17]. However, these predicting models were not sufficient to evaluate the outcome of patients with AC. Therefore, some researchers thought that it would be more beneficial to include some biomarkers such as CK7, MUC1 and MUC5AC; however, this was controversial with regard to the prognostic value of the molecular alterations[18,19,20]. Moreover, too many prognostic factors would be needed to construct a significant model. Therefore, up to now, there is still no effective and suitable model for predicting prognosis. In our study, 2341 patients were extracted from the SEER database to investigate the prognostic factors of CSS. As for the basic characteristics of AC, consistent with other studies, we found that the age at diagnosis of patients with AC mainly ranged from 50–70 years, white people accounted for a majority of the patients and most of the tumors were smaller than 5 cm[21,22]. As for the LNM rate, we found that it was almost as high as the no LNM rate. Actually, it has been reported that the LNM rate of AC is high. John R et al. reported that positive LNM could be found in 45% of T1 patients and 86% of T4 patients[22].

As for the curative treatment of AC, it is estimated that more than 80% of ACs are amenable to resection including surgical and endoscopic removal. For LNM negative lesions, pancreaticoduodenectomy was an indeed curative treatment, while it had a better ability to provide indications for surgery for LNM positive lesions although some lesions were in the early stage[23]. In spite of some notions about the invasion of lymphatic vessels, LNM was an important factor for the determination of treatment methods and to predict prognosis[24]. Hence, the number of harvested LNs was the key factor to determine the optimal LNM state. In our study, we identified the best cut-off value by the KAPS algorithm which has been used in many studies[14,25]. In consistence with some studies[8,11], we found that patients with > 12 examined LNs have more benefit than those who with < 12; however, some studies thought the harvested LNs should be > 17[6,7]. In addition, the multivariate logistic regression analysis showed that tumor size and T stage were independent factors of harvesting LNs, in corroboration with the results of a previous study[26]. With respect to N stage, some studies proposed that the best cutoff point for positive LNs was 0 and 3[10,27], while few studies thought that positive LNs should be divided into 0–1 and ≥ 2 groups[7]. In our

study, the new LNM stage we proposed was N0 (0 positive LNs), N1 (1–4 positive LNs) and N2 (≥ 5 positive LNs), which made a great difference for survival. However, the positive LNs factor was not included in the construction of the nomogram plot because the value of AIC was too large. AIC was considered as an important criterion for variable sieving and has been used in many studies[28,29]. Compared with our model, the TNM staging system earlier was not better for survival prediction, while our model was reasonable and logic by multivariate cox regression analysis and AIC algorithm which can prevent over fitting of the model and ensure the accuracy of model[30]. In our model, we recruited age, T stage, M stage, pathology grade and examined lymph nodes other than TNM stage, avoiding the insufficiency of TNM stage. Naturally, nomogram we conducted performed better than TNM stage, which was demonstrated by ROC curve and DCA analysis.

Our study had some limitations that should be discussed. First, the TNM staging used was the 7th edition rather than the 8th edition, which may influence the results of the comparison between the nomogram and TNM staging models. Hence, it is necessary to perform studies to compare the model constructed by our study with the 8th edition of TNM staging. Second, we excluded many patients who had missing data associated with our collected variables, increasing the selection bias. Third, the variables including examined LNs and positive LNs were diagnosed depending on each doctor in different clinical centers. Finally, the enrolled prognostic parameters were so limited that we could not comprehensively analyze them. Therefore, although this nomogram performed well in the two cohorts, it should be applied with great caution when assessing the risk of 1-, 3- and 5- year survivals. In the future, we will collect our relevant data to incorporate the factors above into further research.

In conclusion, the present study was constructed to investigate the optimal examined and positive LNs. We found that the examined LNs factor was beneficial for the prognosis of the patients, which was more favorable with at least 12 LNs. We also modified the current N staging into three groups based on number of metastatic LNs: N0, no LN metastasis; N1, 1–4 metastatic LNs; and N2, ≥ 5 metastatic LNs. Based on the categories and multivariate analysis, we developed and validated a nomogram with greater benefit for predicting the survival of patients with AC than the TNM staging, which was demonstrated by td-ROC and DCA.

Declarations

Ethics approval and consent to participate:

Ethics approval and consent was obtained from SEER database.

Patient consent for publication:

Not Appliable

Consent for publication:

All study participants provided informed consent.

Data Availability Statement:

The datasets [ANALYZED] for this study can be found in the [Surveillance, Epidemiology, and End Results Program] [https://seer.cancer.gov/].

Conflict of Interest

The authors declare no conflict of interest related to this study.

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Author Contributions:

C.S and Xj.Z contributed to the conception and design of the work. J.Z and Y.Z contributed to design, data analysis, editing the manuscript and critical revision of the manuscript. X.H contributed to data analysis. J.Z and X.Z contributed to data acquisition. All authors read and approved the final manuscript.

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Tables

Table 1

Patients’ demographics, clinical characteristics at diagnosis

Variables	Total (%)	2004-2009	2010-2015	P Value
n	2341	965(48.25%)	1376(51.75%)	
Age				0.476
<50	264(11.28%)	118(12.23%)	146(10.61%)	
50-70	1279(54.63%)	522(54.09%)	757(55.01%)	
>70	798(34.09%)	325(33.68%)	473(34.38%)	
Race				0.254
White	1784(76.21%)	752(77.93%)	1032(75%)	
Black	176(7.52%)	66(6.84%)	110(7.99%)	
Other	381(16.28%)	147(15.23%)	234(17.01%)	
Sex				0.333
Female	1013(43.27%)	429(44.46%)	584(42.44%)	
Male	1328(56.73%)	536(55.54%)	792(57.56%)	
Pathology Grade				0.406
Well	254(10.85%)	101(10.47%)	153(11.12%)	
Moderately differentiated	1259(53.78%)	506(52.44%)	753(54.72%)	
Poorly	810(34.6%)	352(36.48%)	458(33.28%)	
Undifferentiated	18(0.77%)	6(0.62%)	12(0.87%)	
Lymph node Metastasis				0.404
NO	1041(44.47%)	439(45.49%)	602(43.75%)	
Yes	1300(55.53%)	526(54.51%)	774(56.25%)	
Metastasis				0.296
No	2278(97.31%)	935(96.89%)	1343(97.6%)	
Yes	63(2.69%)	30(3.11%)	33(2.4%)	
Tumor size				0.79
≤2cm	1127(48.14%)	470(48.7%)	657(47.75%)	
<=3cm	620(26.48%)	256(26.53%)	364(26.45%)	
<=5cm	436(18.62%)	171(17.72%)	265(19.26)	
>5cm	158(6.75%)	68(7.05%)	90(6.54%)	

Examined LNs count				0.000
<=12	1034(44.17%)	527(54.61%)	507(36.85%)	
>12	1306(55.79%)	438(45.39%)	869(63.15%)	
T stage				0.013
T1	292(12.47%)	138(14.3%)	154(11.19%)	
T2	668(28.53%)	247(25.6%)	421(30.6%)	
T3	737(31.48%)	319(33.05%)	418(30.38%)	
T4	644(27.51%)	261(27.05%)	383(27.83%)	
Positive LNs count				0.437
0	1049(44.81%)	445(46.11%)	604(43.9%)	
1-4	852(36.39%)	349(36.17%)	503(36.56%)	
>=5	440(18.8%)	171(17.72%)	269(19.55%)	
7th TNM stage				0.563
I	604(25.8%)	244(25.28%)	360(26.16%)	
II	1055(45.06%)	442(45.8%)	613(44.55%)	
III	618(26.39%)	248(25.7%)	370(26.89%)	
IV	64(2.73%)	31(3.21%)	33(2.4%)	

Table 2

Univariate and Multivariate logistic regression analysis of ampulla cancer patients for examined LNs

Variables	Univariate analysis		Multivariate analysis	
Age				
<50	Reference	-		
50-70	0.909(0.694-1.19)	0.487		
>70	0.789(0.595-1.046)	0.099		
Race				
White	Reference	-		
Black	1.073(0.784-1.467)	0.66		
Other	1.01(0.808-1.262)	0.931		
Sex				
Male	Reference	-		
Female	1.039(0.881-1.225)	0.648		
Pathology Grade		0.039		0.067
Well	Reference	-	Reference	-
Moderately differentiated	1.253(0.957-1.642)	0.012	1.051(0.832-1.142)	0.32
Poorly	1.248(0.941-1.656)	0.03	1.121(0.901-1.456)	0.193
Undifferentiated	1.938(0.706-5.323)	0.63	1.438(0.876-6.23)	0.43
Year of diagnosis				0.000
2004-2009	Reference	-	Reference	-
2010-2015	2.062(1.744-2.438)	0.000	2.056(1.737-2.433)	
Tumor size				0..018
≤2cm	Reference	-	Reference	-
<=3cm	1.224(1.004-1.492)	0.045	1.187(0.969-1.455)	0.098
<=5cm	1.159(0.927-1.448)	0.035	1.284(0.858-1.546)	0.045
>5cm	1.435(1.019-2.019)	0.039	1.76(1.018-1.978)	0.037
T stage				
T1	Reference	-	Reference	-

T2	1.354(1.028-1.784)	0.031	1.249(0.943-1.655)	0.012
T3	1.321(1.007-1.733)	0.045	1.425(1.101-1.746)	0.013
T4	1.602(1.213-2.117)	0.001	1.737(1.23-2.443)	0.009

Table 3

Univariate and Multivariate cox regression analysis of ampulla cancer patients for CSS

Variables	Univariate analysis		Multivariate analysis	
Age		0.000		
<50	Reference	-	Reference	-
50-70	1.414(1.127-1.774)	0.003	1.493(1.188-1.876)	0.001
>70	1.752(1.388-2.211)	0.000	1.896(1.498-2.4)	0.000
Race		0.094		
White	Reference	-		
Black	1.252(0.998-1.57)	0.052		
Other	0.938(0.787-1.117)	0.470		
Sex				
Male	Reference	-		
Female	0.906(0.799-1.027)	0.122		
Pathology Grade		0.000		
Well	Reference	-	Reference	-
Moderately differentiated	1.594(1.248-2.035)	0.000	1.427(1.116-1.826)	0.005
Poorly	2.491(1.946-3.19)	0.000	1.774(1.379-2.282)	0.000
Undifferentiated	2.519(1.261-5.034)	0.009	1.283(0.636-2.587)	0.486
Metastasis				
No	Reference	-	Reference	-
Yes	2.416(1.79-3.26)	0.000	1.564(1.146-2.136)	0.005
Tumor size				
≤2cm	Reference	-	Reference	-
<=3cm	1.305(1.126-1.513)	0.000	1.059(0.911-1.23)	0.458
<=5cm	1.3(1.1-1.537)	0.002	0.947(0.795-1.129)	0.545
>5cm	1.234(0.962-1.582)	0.098	0.949(0.736-1.225)	0.689
T stage		0.000		
T1	Reference	-	Reference	-
T2	1.331(1.022-1.734)	0.034	1.175(0.9-1.534)	0.236
T3	2.554(1.993-3.273)	0.000	1.87(1.448-2.415)	0.000

T4	3.476(2.713-4.453)	0.000	2.17(1.67-2.82)	0.000
Positive nodes count				
0	Reference	-	Reference	-
1-4	2.408(2.075-2.796)	0.000	1.583(1.042-2.561)	0.043
>=5	3.782(3.203-4.465)	0.000	2.21(1.704-3.212)	0.003
Examined LNs count				
<=12	Reference	-	Reference	-
>12	0.819(0.724-0.927)	0.002	0.692(0.609-0.786)	0.000
Lymph node Metastasis				
NO	Reference	-	Reference	-
Yes	2.813(2.45-3.229)	0.000	1.843(0.685-4.958)	0.226

Table 4

Accuracy of the prediction score of the nomogram and TNM stage for estimating prognosis of AC patients.

Variable	Value (95%CI)	
	Internal validation	External validation
C index for nomogram	0.686(0.584-0.773)	0.713(0.651-0.784)
C index (bootstrap corrected)	0.674	0.698
C index for TNM stage	0.616(0.533-0.754)	0.647(0.551-0.719)
C index (bootstrap corrected)	0.615	0.643
1 year AUC for nomogram	0.719(0.634-0.781)	0.698(0.625-0.784)
3 year AUC for nomogram	0.788(0.672-0.833)	0.764(0.709-0.811)
5 year AUC for nomogram	0.782(0.653-0.858)	0.774(0.701-0.813)
1 year AUC for TNM stage	0.596(0.537-0.702)	0.658(0.605-0.704)
3 year AUC for TNM stage	0.673(0.601-0.714)	0.717(0.659-0.801)
5 year AUC for TNM stage	0.689(0.633-0.768)	0.677(0.601-0.713)

Figures

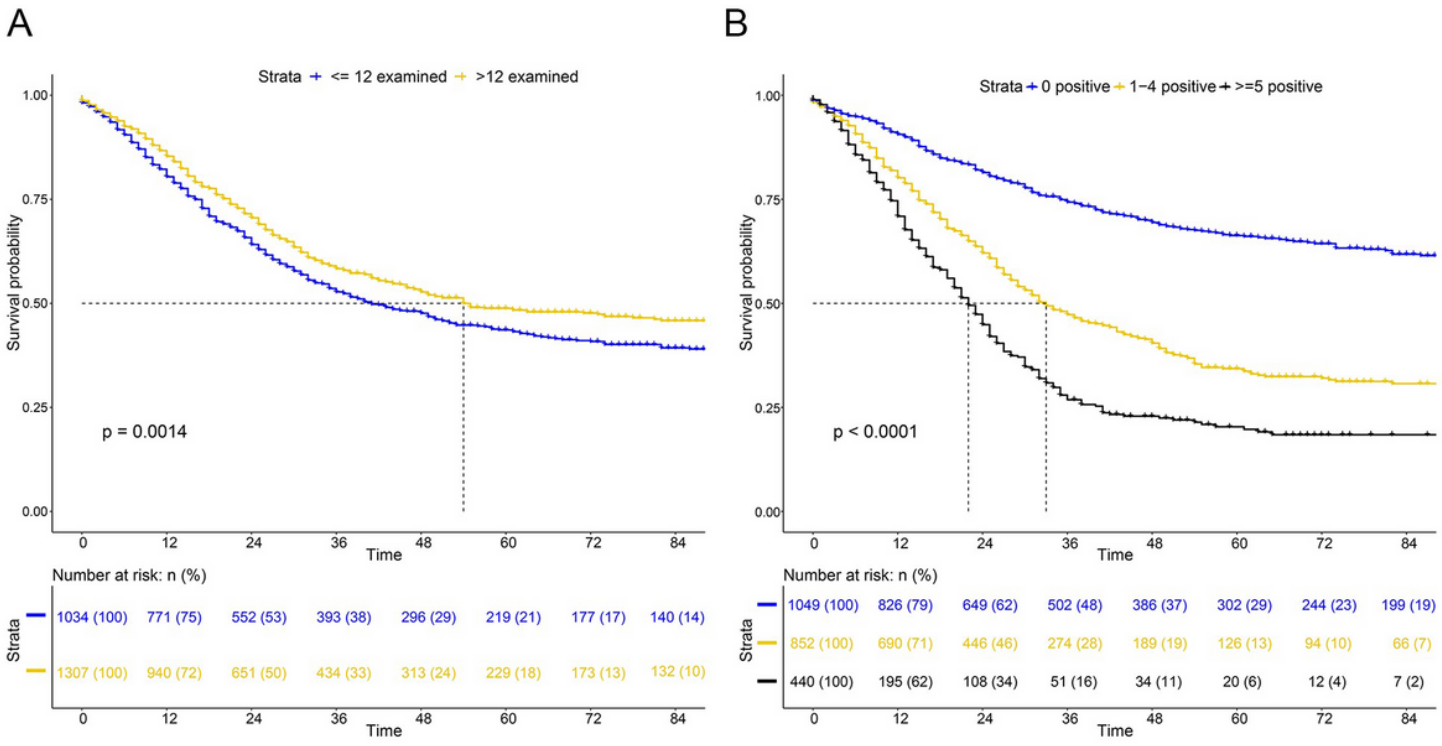

Figure 1

Kaplan-Meier survival analysis according to the number of examined LNs and positive LNs. (A) examined LNs, (B) positive LNs.

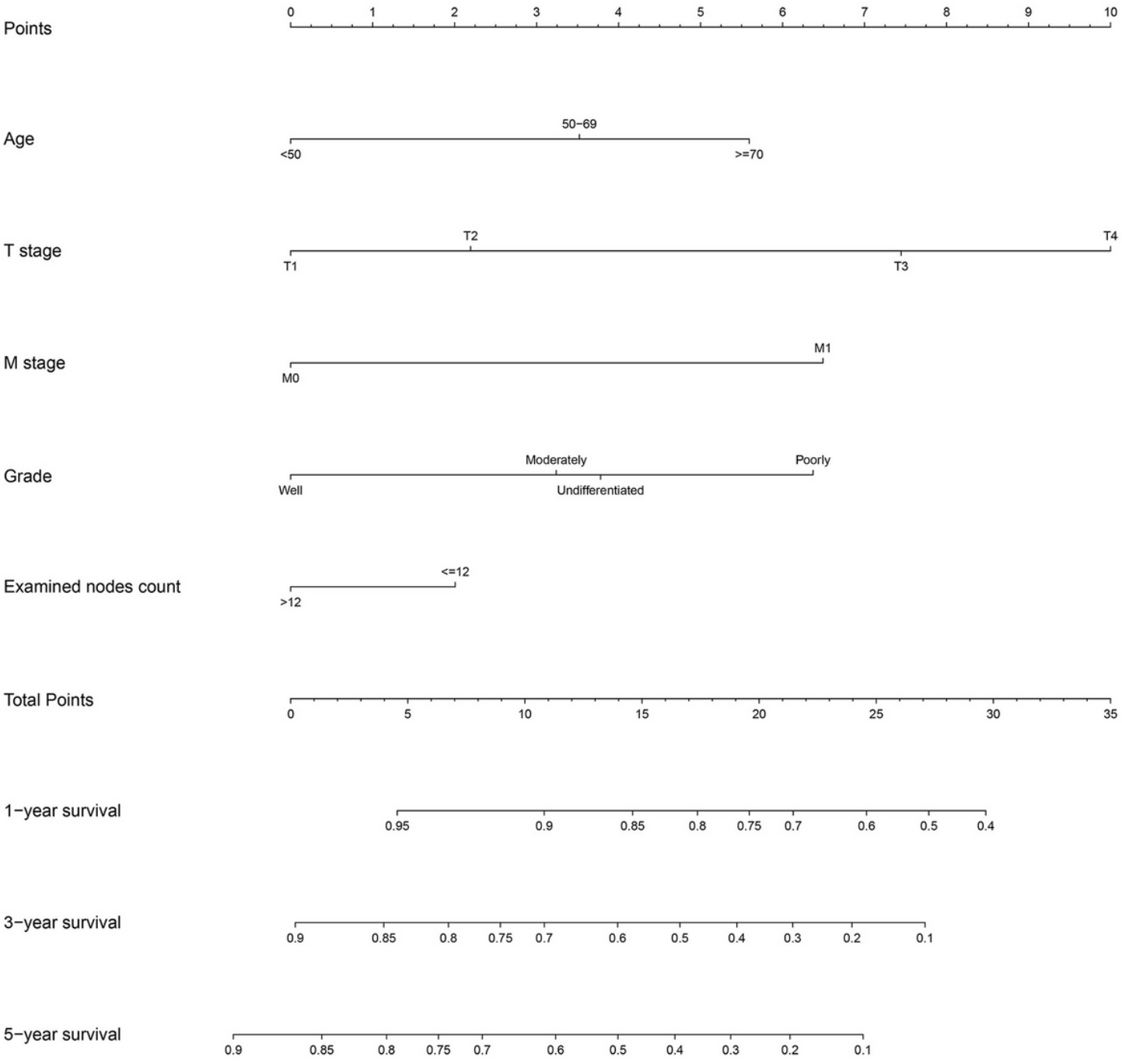

Figure 2

Nomogram predicted 1-, 3- and 5-year cancer specific survival for patients with resected AC.

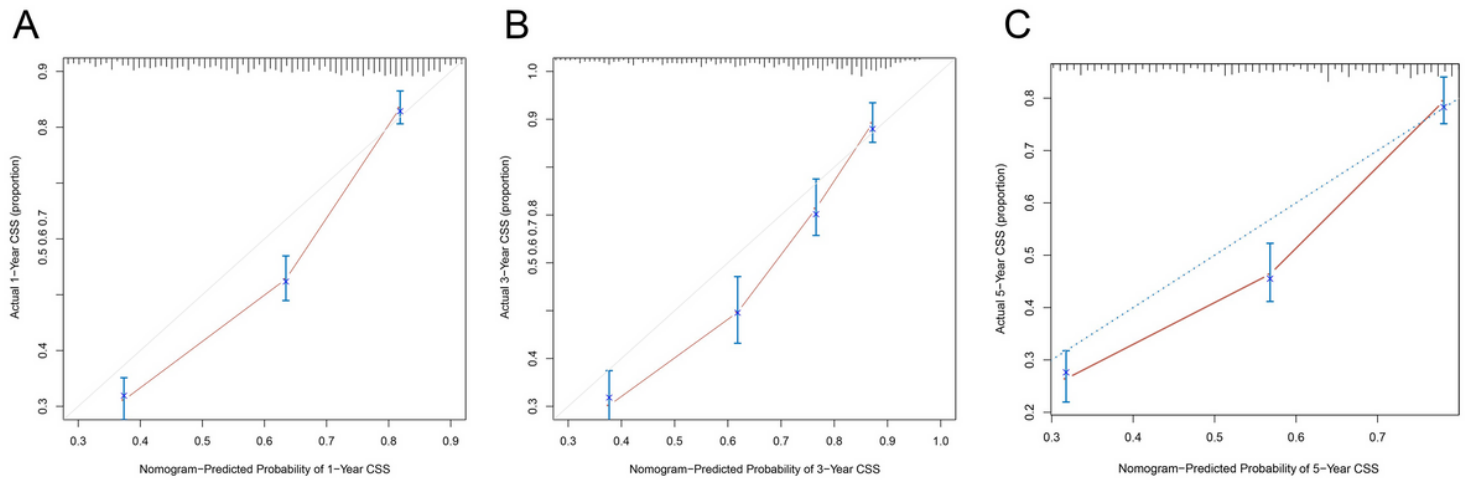

Figure 3

The calibration curves at 1-, 3- and 5-year point in the 2004–2015 cohort. (A) 1-year survival. (B) 3-year survival. (C) 5-year survival. Nomogram-predicted CSS is plotted on the x-axis; cancer specific survival is plotted on the y-axis.

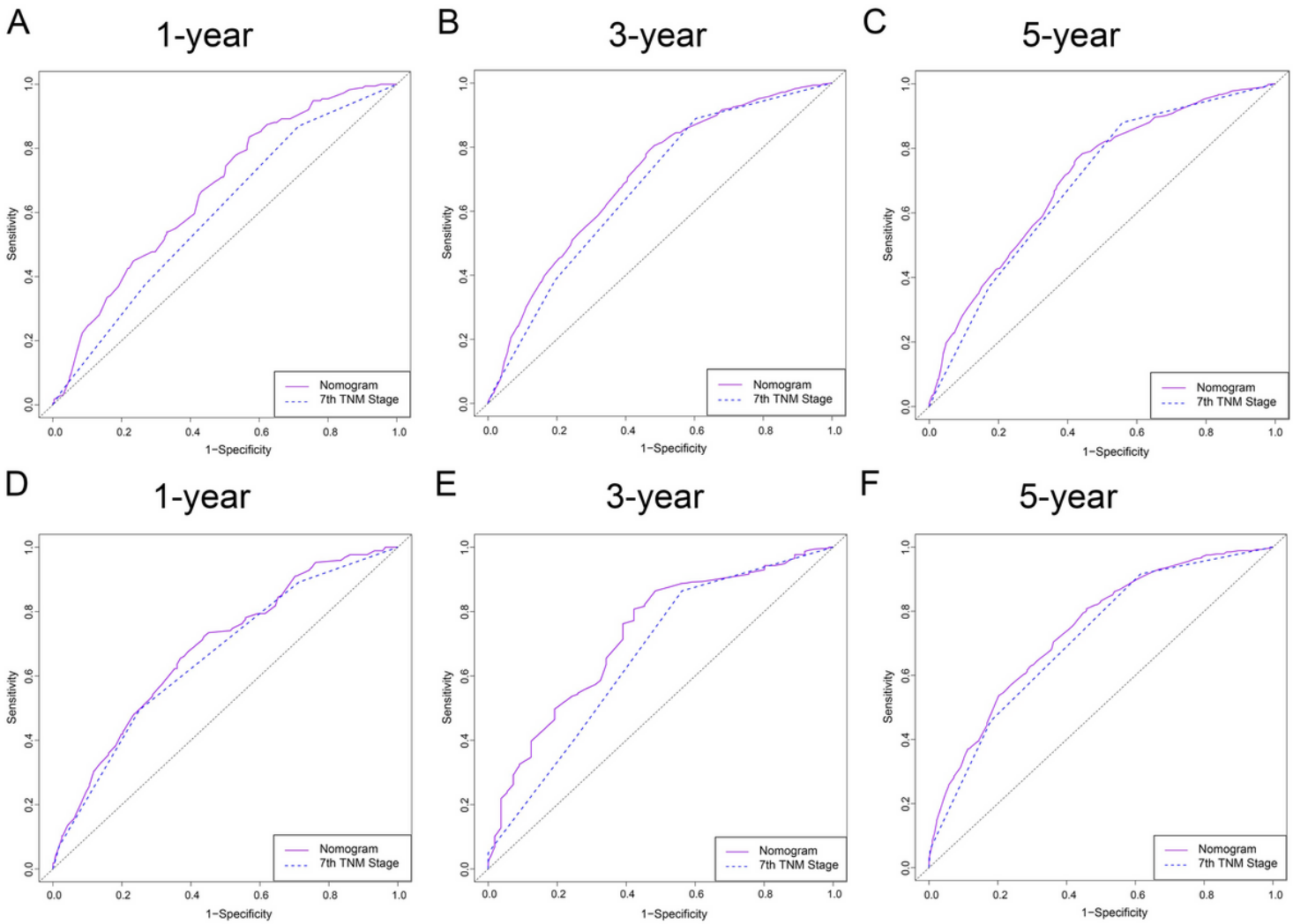

Figure 4

ROC curve of the Nomogram and 7th TNM Stage in prediction of prognosis of patients from 2004 to 2015. (A-C) ROC curve for 1-, 3- and 5- year point in 2004-2009 cohort. (D-F) ROC curve for 1-, 3- and 5- year point in 2010-2015 cohort.

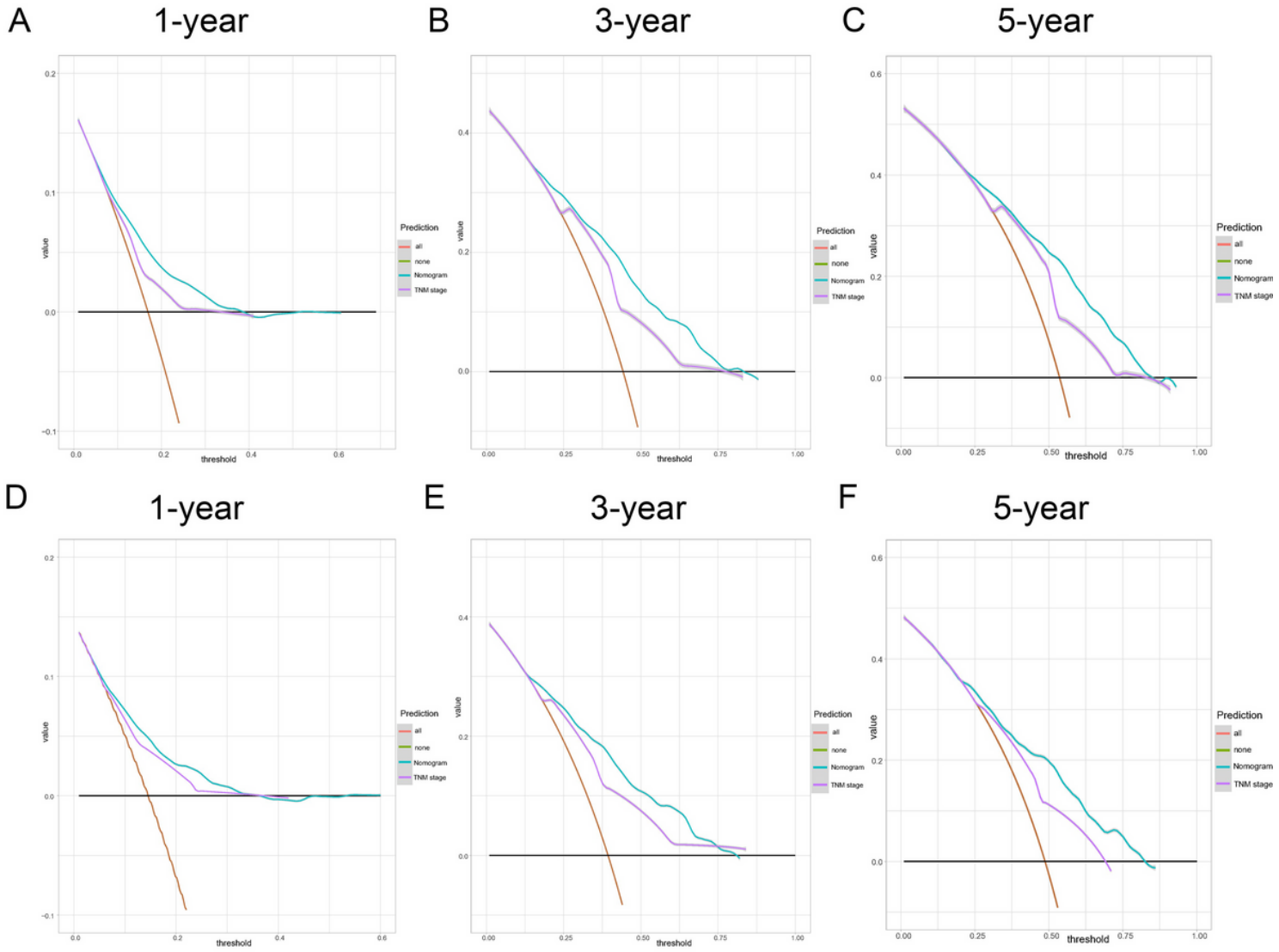

Figure 5

Decision curve analysis for the Nomogram and the model 7th TNM Stage in prediction of prognosis of patients. (A-C) 1-, 3- and 5- year point in 2004-2009 cohort. (D-F) 1-, 3- and 5- year point in 2010-2015 cohort.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- supplementary.SupplementaryFigure1.docx