Nomogram predicts the overall survival of patients with Glioma

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Research

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Abstract

Aim Our study aimed to establish a nomogram to predict the cancer-specific surviva (CSS) of patients with Glioma.

Patients and methods Patients diagnosed with glioma between 2004 and 2016 were collected from the SEER database. On the basis of the logistic regression model, the nomogram was established, the C-index was used to evaluate the accuracy of the nomogram, and the Decision Curve Analysis was used to evaluate the clinical use of the nomogram.

Results 2626 eligible patients were randomly divided into training group (n=1864) and verification group (n=762). Nomogram had better discrimination ability, the C index of the training cohort was 0.74, and the C index of the verification cohort was 0.736. This new predictive model has shown better discriminative ability and greater benefits in both training and validation cohorts to predict CSS in patients with Glioma.

Conclusion A nomogram was constructed to predict the CSS of Glioma patients at 1, 3, and 5 years. The verification showed that the nomogram had better discrimination and calibration ability, indicating that the nomogram can be used to predict the CSS of Glioma patients and guide the treatment of Glioma patients.

1. Introduction

Glioma is a primary intracranial tumor with poor prognosis, which is highly aggressive, accounting for about 81% of malignant tumors, and has a high morbidity and mortality [1, 2]. As the second most common primary central nervous system tumor in the world,

According to histological types, astrocytoma, glioblastoma and oligodendroglioma are clinically classified [3–5]. Without systematic treatment, most patients are diagnosed and die within a year. At present, surgery is still the main treatment method, combined with radiotherapy, chemotherapy, immunotherapy, etc., which can delay disease recurrence to a certain extent and prolong the survival period [6–9]. The prognosis of patients various with different treatment options. For clinicians, it is very important to accurately predict the CSS and choose the best treatment method. However, there is no scoring system on the relationship between clinicopathological factors and CSS in glioma patients. Therefore, the purpose of this study is to identify independent factors related to CSS and establish a nomogram to predict 1, 3, and 5 CSS of glioma patients. The 5-year CSS provides individualized survival prediction and treatment plans for glioma patients.

2. Patients And Methods

This study used the National Cancer Institute database (The Surveillance, Epidemiology, and End Results), which records the morbidity, mortality, and disease status of approximately 30% of millions of patients with malignant tumors in the United States. The SEER*Stat software version 8.3.5 was used to

extract the data of patients diagnosed with glioma from 2004 to 2016 based on the SEER database. The training cohort consisted of the following patients: the third edition of the International Classification of Diseases in Oncology (ICD-O-3). The exclusion criteria were: (1) patients without pathological diagnosis; (2) patients with missing or incomplete clinical pathological data. Because the SEER study data are publicly available, this study does not require the approval and informed consent of the institutional review committee. All authors have signed the authorization form and obtained the permission of the SEER organization to access and use the data set.

2.1 Data collection

The clinicopathological characteristics used in this study are: time at diagnosis, age at diagnosis, gender, race, Marital status, Insurance status, primary site, histological grade, summary stage, tumor size, chemotherapy, surgery for primary site and survival months .

2.2 Statistical Analysis

SPSS software version 22 and the version 3.4.2 software were used for statistical analysis. T test was used for comparison between two groups, and chi-square test was used for mandatory categorical variables. Single factor logistic regression analysis analyzes the relationship between CSS and clinicopathological factors. In multivariate analysis, variables deemed significant were further analyzed to determine independent risk factors for CSS. The HR and related 95% confidence interval (CI) were calculted, and the independent risk factors identified in the multivariate analysis were included in the Nomogram prediction method for glioma CSS prediction, and the C index and calibration curve were used to evaluate the performance of the nomograph. Decision curve analysis (DCA) was used to evaluate the clinical application of nomogram, and $P < 0.05$ was used as a sign of Statistical significance.

3. Results

3.1 characteristics of Glioma

A total of 2626 patients were enrolled in this study, all of whom were diagnosed as Glioma. The 2626 patients were assigned to two different cohorts, including 1864 in the training cohort (70.98%) and 762 in the verification cohort (29.02%). There was no statistical differences among variables between the training and validation groups ($P > 0.05$), Table 1 shows the demographic and pathological characteristics of Glioma patients.(Table 1.)

Table 1
Clinicopathological characteristics of all patients

Characteristics	Training set (n = 1864)	Validation set (n = 762)	P value
Year of diagnosis, n (%)			0.761
2004–2008	747 (40.1)	305 (40.0)	
2009–2012	610 (32.7)	242 (31.8)	
2013–2016	507 (27.2)	215 (28.2)	
Age (years), n (%)			0.465
<60	1381 (74.1)	575 (75.5)	
≥60	483 (25.9)	187 (24.5)	
Sex, male, n (%)	1045 (56.1)	441 (57.9)	0.395
Race, n (%)			0.399
White	1539 (82.6)	640 (84.0)	
Black	167 (9.0)	63 (8.3)	
Others	158 (8.4)	59 (7.7)	
Marital status at diagnosis, n (%)			0.556
Married	862 (46.2)	362 (47.5)	
No/unknown	1002 (53.8)	400 (52.5)	
Insurance status, n (%)			0.168
Insured	1363 (73.1)	537 (70.5)	
No/unknown	501 (26.9)	225 (29.5)	
Primary site, n (%)			0.465
Cerebrum	92 (4.9)	34 (4.5)	
Frontal lobe	489 (26.2)	212 (27.8)	
Temporal lobe	237 (12.7)	99 (13.0)	
Parietal lobe	141 (7.6)	63 (8.3)	
Occipital lobe	34 (1.8)	8 (1.0)	
Ventricle, NOS	10 (0.5)	10 (1.3)	
Cerebellum, NOS	32 (1.7)	10 (1.3)	
C- **index for CSS in test set 0.740 95%CI (0.717–0.763); in validation set 0.736 95%CI (0.701–0.771)**			

Characteristics	Training set (n = 1864)	Validation set (n = 762)	P value
Brain stem	561 (30.1)	223 (29.3)	
Overlapping lesion of brain	181 (9.7)	63 (8.3)	
Brain, NOS	87 (4.8)	40 (5.2)	
Histological grade, n (%)			0.697
Well differentiated	1102 (59.1)	464 (60.9)	
Moderately differentiated	163 (8.7)	53 (7.0)	
Poorly differentiated	139 (7.5)	60 (7.9)	
Undifferentiated	460 (24.7)	185 (24.3)	
Summary stage, n (%)			0.171
Localized	1519 (81.5)	643 (84.4)	
Regional	326 (17.5)	108 (14.2)	
Distant	19 (1.0)	11 (1.4)	
Tumor size, n (%)			0.227
<3cm	862 (46.2)	327 (42.9)	
3-5cm	537 (28.8)	238 (31.2)	
≥5cm	465 (24.9)	197 (25.9)	
Chemotherapy, n (%)			0.316
Yes	1217 (65.3)	474 (62.2)	
No/unknown	647 (34.7)	1288 (37.8)	
Surgery for primary site, n (%)			0.340
Yes	928 (49.8)	395 (51.8)	
No/unknown	936 (50.2)	367 (48.2)	
Survival months	17.0 (7.0, 49.0)	17.0 (8.0, 46.0)	0.516
OS, n (%)	1236 (66.3)	482 (36.7)	0.135
CSS, n (%)	1003 (53.8)	402 (52.8)	0.624
C- **index for CSS in test set 0.740 95%CI (0.717–0.763); in validation set 0.736 95%CI (0.701–0.771)**			

3.2 Independent prognostic factors in the training set

Single factor analysis screened risk factors, and all these factors entered multivariate logistic regression analysis. The single factor results of CSS indicate that age > 60 years old, married ($P < 0.001$), fortal lobe ($P < 0.001$), distant summary stage ($P < 0.001$), tumor size > 3cm ($P < 0.001$), surgery ($P < 0.001$)) patients are more likely to have a higher mortality rate. Multivariate analysis of CSS showed that age > 60 years old, married ($P = 0.025$), fortal lobe ($P = 0.001$), Temporal lobe ($P = 0.043$), regional ($P < 0.001$), distant ($P = 0.008$), surgery Of patients have a higher risk of death (Table 2).

Table 2
Univariate and multivariate analyses of factors associated with CSS

	Univariate analysis		Multivariate analysis	
	HR (95%CI)	P	HR (95%CI)	P
Age (years)				
≥60	1.35 (0.86–2.13)	0.190		
<60	Ref.	-		
Sex, male	1.31 (0.81–2.09)	0.269		
Primary site				
Left colon	1.48 (0.88–2.49)	0.140		
Right colon	1.67 (0.94–2.95)	0.078		
Rectum	Ref.	-		
Family history of cancer	7.14 (0.98–51.35)	0.054		
Histological grade				
Well differentiated	Ref.	-		
Moderately differentiated	1.14 (0.60–2.18)	0.683		
Poorly differentiated	2.04 (0.84–4.92)	0.114		
Tumor size				
<2cm	Ref.	-		
2-5cm	1.14 (0.35–3.69)	0.824		
≥5cm	1.45 (0.44–4.73)	0.540		
Vascular invasion				
Yes	1.13 (0.63–2.03)	0.671		
No	Ref.	-		
Circumferential resection margin				
Yes	1.42 (0.23–10.08)	0.653		
No	Ref.	-		
T stage				
T1	Ref.	-	Ref.	-
T2	1.54 (0.0.38–6.53)	0.556	1.60 (0.34–7.44)	0.549

	Univariate analysis		Multivariate analysis	
	HR (95%CI)	P	HR (95%CI)	P
T3	1.67 (0.37–7.62)	0.510	1.17 (0.26–5.19)	0.836
T4	7.17 (1.73–29.65)	0.007	3.92 (1.03–16.91)	0.038
N stage				
N0	Ref.	-	Ref.	-
N1	0.68 (0.31–1.53)	0.234	0.64 (0.25–1.61)	0.344
N2	1.56 (0.72–3.43)	0.125	0.58 (0.20–1.69)	0.320
N3	2.70 (1.15–5.88)	0.010	0.78 (0.26–2.32)	0.655
TNM stage				
Stage I	Ref.	-	Ref.	-
Stage II	1.59 (0.54–4.73)	0.403	1.12 (0.32–3.93)	0.862
Stage III	4.96 (1.80-13.69)	0.002	3.05 (1.07–10.67)	0.040
Adjuvant chemotherapy				
Yes	0.66 (0.16–2.71)	0.569		
No	Ref.	-		
Radiotherapy				
Yes	0.46 (0.28–0.76)	0.002	0.71 (0.40–1.25)	0.231
No	Ref.	-	Ref.	-
CSII				
Low	Ref.	-	Ref.	-
Interrmediate	4.62 (2.03–10.54)	< 0.001	3.37 (1.53–7.43)	0.003
High	15.62 (6.95–35.08)	< 0.001	10.11 (4.64–22.03)	< 0.001

3.3 Construction and verification of survival line graph

Based on the CSS-based multivariate COX results (Table 2), age, marital status, grade, primary site, surgery and summary stage are finally included in the nomogram. Patients' 1 -, 3 -, and 5-year overall survival predictions were estimated by calculating a weighted total score for each variable (Fig. 1). The performance of the Nomogram has been verified internally through discrimination and calibration methods. The C index of the training set is 0.74 (95% CI: 0.717–0.763), and the C index of the validation

set is 0.736 (95% CI: 0.701–0.771), indicating that the nomogram has better discrimination ability. The calibration chart shows a good correlation between the observed operating system and the nomogram predicted operating system (Fig. 2).

3.4 Clinical application of the model

Decision curve analysis (DCA) mainly evaluates predictive models from the perspective of clinical consequences. When the score is 0–1, patients can obtain a greater net benefit by using the Nomograph to predict glioma survival (Fig. 3).

3.5 The overall survival of the nomogram with different score

The patients were divides into three groups according to the scores of the nomogram by X title, and the more scores, the poorer of prognosis with patients, this indicated the value of the scores of nomogram (Fig. 4 and Fig. 5).

4. Discussion

Glioma is a collective term for malignant tumors derived from glial cells and neuronal cells in the nervous system. Primary tumors of the central nervous system, known as gliomas, occur in 18.7 out of every 100,000 people in the United States.There are 7 cases per 100,000 people in the world, and more than half of the patients are glioblastoma, and their five-year survival period is less than 5%[10–12]. Genetic diseases (type I neurofibromatosis, tuberculous sclerosis), electromagnetic radiation, etc may be related to the generation of gliomas[13, 14]. The symptoms caused by glioma are mainly related to the size, location and growth rate of the tumor. Typical clinical symptoms include headache, nausea, vomiting, blurred vision etc may be accompanied by symptoms such as decreased brain function, memory loss, personality changes, visual impairment, and urinary incontinence [15–18].

Age, physical status, tumor registration, histological type, and scope of surgical resection are all important prognostic factors affecting the survival of patients with glioma[19, 20]. Because glioma is highly aggressive [21] and located in the skull, it is difficult to predict the patient's CSS due to the complexity of the condition and location. In addition, there is currently no CSS scoring system specifically for the clinical factors of glioma, making it difficult to accurately predict the CSS of glioma patients. Therefore, we developed a CSS prediction system for the clinicopathological factors of glioma.

Our research demostrated that there are more patients under 60 years old, male, white, well differentiated, tumor size < 3cm, and undergoing surgery. The analysis of the prognostic factors of the disease showed that, except for age, martial status, grade, primary site, surgery, summary stage, other factors (chemotherapy, tumor size, etc.) have no significance in CSS prediction. Based on our research, a prognostic nomogram was developed, which can be used to predict the possibility of survival assessment. In the univariate and multivariate models, the patients who have undergone surgery have achieved good CSS, so it is recommended that patients undergo surgery as much as possible to improve survival.

In short, this is a study that reported the demographics, clinicopathological characteristics, and prognostic factors of gliomas and established a reliable nomogram to predict CSS in patients. This study showed that age, martial status, grade, primary site, surgery, and summary stage are independent prognostic factors affecting CSS in patients with glial pathways. However, this study also had certain limitations. For example, because the SEER database does not fully include unmeasured confounders that contribute to survival bias, such as comorbidities, different treatment options may result.

Abbreviations

CSS cancer-specific surviva

SEER Surveillance, Epidemiology, and End Results

ICD International Classification of Diseases

SPSS Statistical Product and Service Solutions

CI confidence interval

HR risk ratio

DCA Decision curve analysis

Declarations

Ethics approval and consent to participate

The data comes from the SEER database and belongs to the OA database, so there is no need for ethics approval and consent to participate .

Agree to publish

All authors agree to publish.

Data availability

The datasets generated during and/or analysed during the current study are available from the corresponding authors on reasonable request.

Conflict of interest

The authors have no conflicts of interest to declare.

funds

There is No funds.

Author's contribution

Junming Xu wrote the article .

Honglin Li downloads data and plots.

Yuanyuan zou provides article ideas and structure.

Chunjiao Yu modified the article.

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Figures

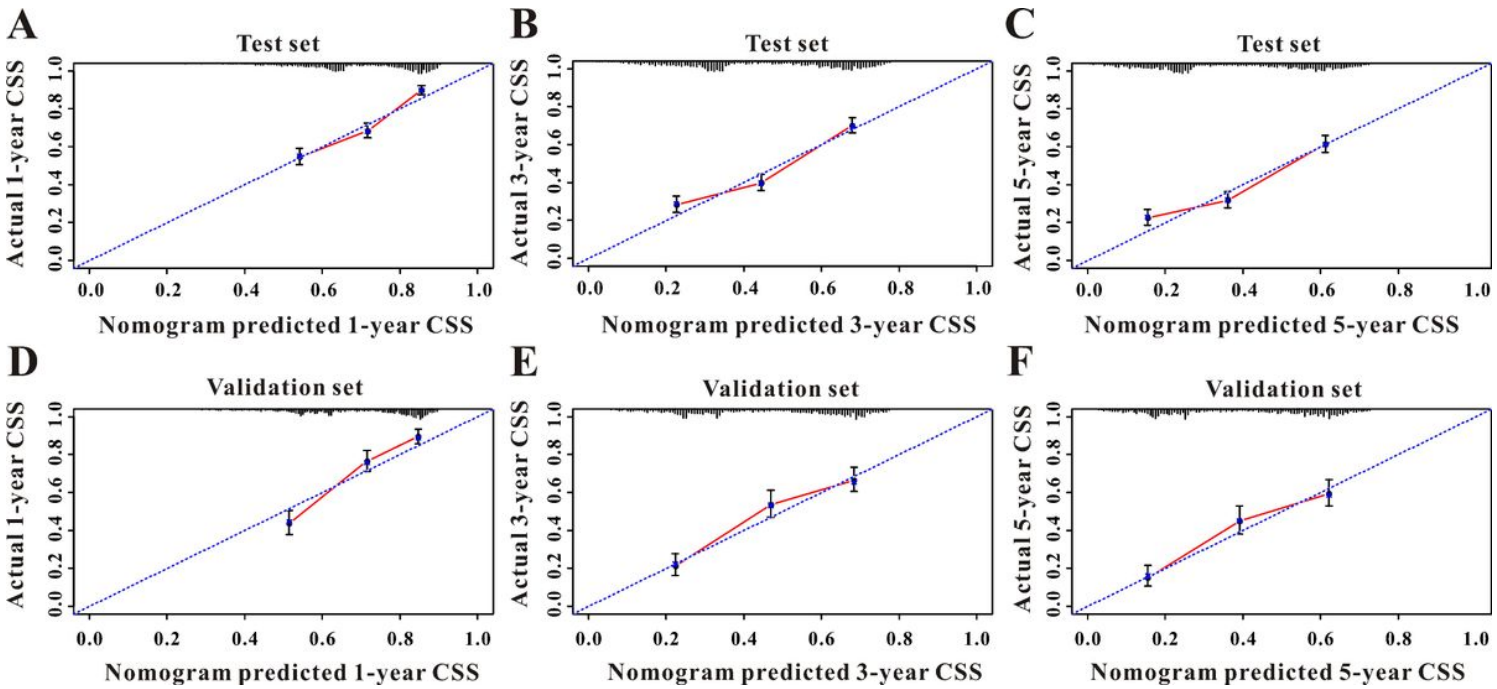

Figure 1

A nomogram for predicting the 1,3,5-year CSS of Glioma

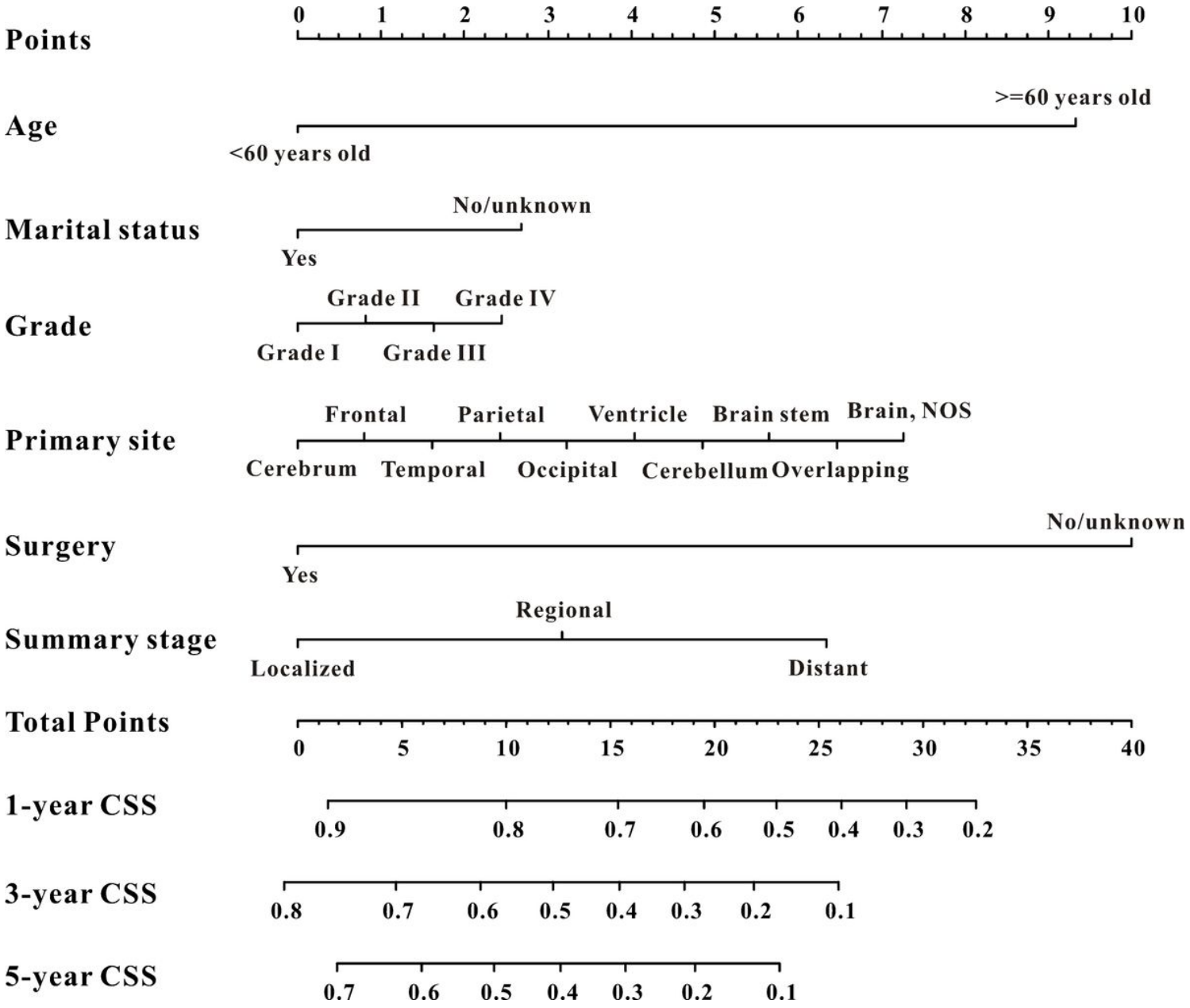

Figure 2

Nomogram model calibration curves

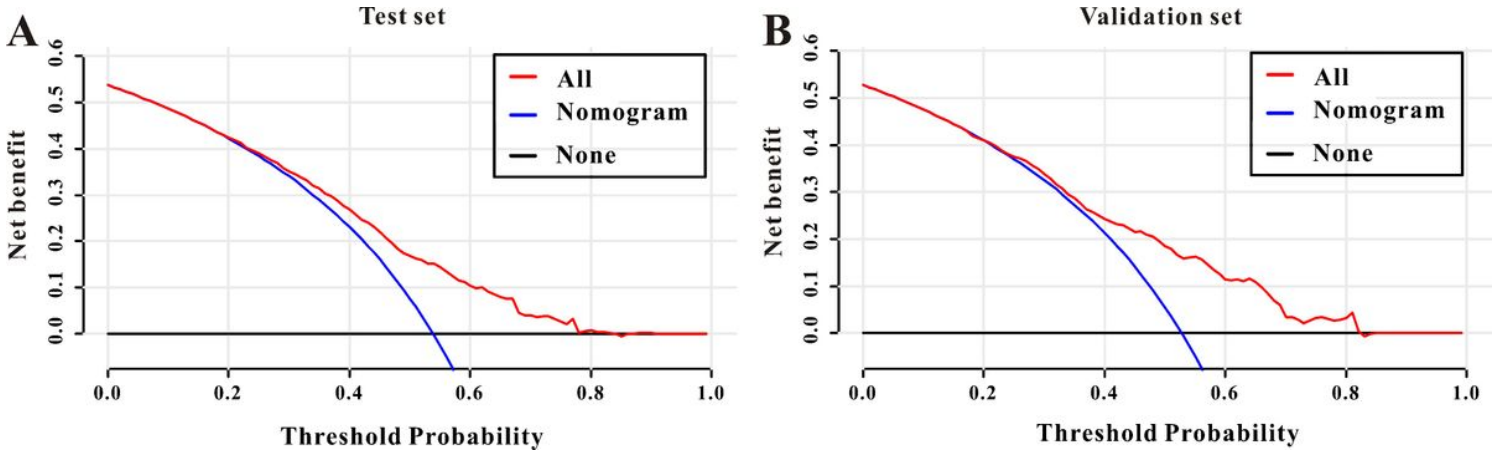

Figure 3

Decision curve analysis for nomogram. The y-axis represents net benefit. The X-axis shows the threshold probability

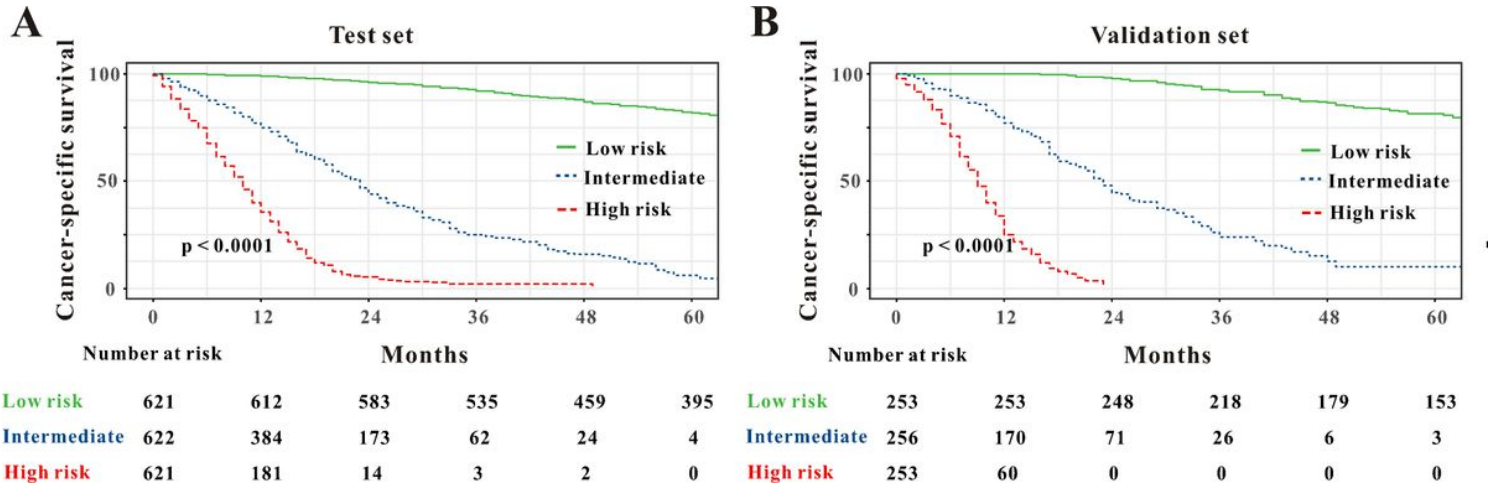

Figure 4

The overall survival of the nomogram with different score (A and B)

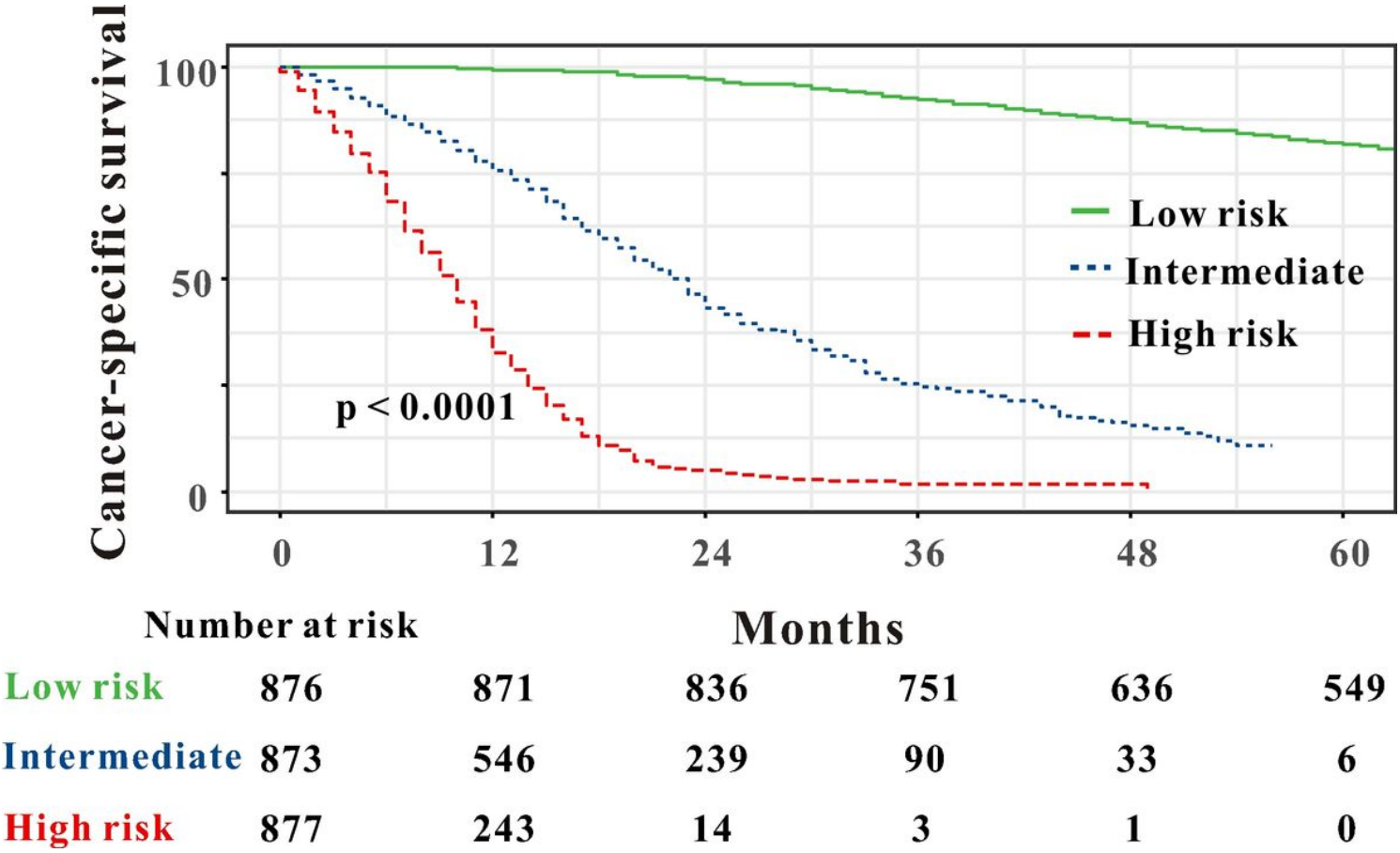

Figure 5

The overall survival of the nomogram with different score