A nomogram for predicting overall survival in patients with Merkel cell carcinoma: A population-based analysis

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Research

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Abstract

Background: Merkel cell carcinoma (MCC) is a rare neuroendocrine skin cancer with increasing incidence and poor prognosis. We sought to develop and validate a nomogram to estimate overall survival (OS) of MCC patients.

Methods: 1863 MCC patients between 2010-2015 from the Surveillance, Epidemiology and End Results (SEER) database were randomly divided into the training and validation cohort. Independent prognostic factors determined by Cox regression analysis in the training cohort were used to establish a nomogram. We evaluated prognostic performance using the concordance index (C-index), area under receiver operating characteristic curve (AUC) and calibration curves. Decision curve analysis (DCA), net reclassification index (NRI) and integrated discrimination improvement (IDI) were used to compared the the nomogram's clinical utility with that of the staging system.

Results: eight independent prognostic factors were incorporated in the nomogram. The C-index of the nomogram was 0.744, which was superior to the C-index of AJCC TNM Stage (0.659). The AUC was greater than 0.75 and the calibration plots of this model exhibited good performance. Additionally, the positive NRI and IDI of nomogram versus the staging system illustrated that the nomogram had better predictive accuracy than the staging system (P<0.001) and the DCA showed great clinical usefulness of the nomogram. MCC patients were perfectly classified into three risk groups by the nomogram, showing better discrimination than the staging system.

Conclusions: We developed and validated a nomogram to assist clinicians in evaluating prognosis of MCC patients.

Introduction

Merkel cell carcinoma (MCC) is a rare neuroendocrine skin cancer that often presents as a solitary cutaneous or subcutaneous nodule on sun-exposed areas in the advanced age population[1]. Immunosuppression, chronic sun exposure and advanced age are major risk factor[2-4]. Approximately 80% MCC cases are associated with Merkel cell polyomavirus (MCPyV) infection and the remaining 20% are associated with chronic sun exposure[5-7]. Since the first description by Toker in 1972[8], the incidence of MCC increased rapidly and this trend was sustained into the new millennium[9-12]. The increased incidence was considered to be related to reduced misdiagnosis as the new pathological diagnosis technology of cytokeratin-20 staining was in introduced in the 1990s[13]. Besides, the increase in at-risk population of elderly people, immunosuppression individuals is another important risk factor[12,14].

MCC is highly malignant and aggressive, with more than 1/3 patients dying from MCC, which is the second leading cause of skin-cancer death following melanoma[15,16]. Local failure, regional recurrence as well as distant metastases remain primary causal factors of the high mortality and poor prognosis[17,18]. Approximately 26%-36% MCC patients have nodal diseases and 6-16% of patients present with distant

metastases at the time of diagnosis[19]. During their disease course, up to 25-50% patients present local or locoregional recurrence depending on their stages and nodal diseases[20-23]. Surgery is the the primary treatment modality for MCC. If surgery is not feasible, radiation therapy is an effective strategy to control disease. Chemotherapy was the only treatment option for advanced-stage or refractory MCC patients before immunotherapies was demonstrated to be effective in MCC in several recent clinical trials[19]. However, despite major advancements in the understanding of MCC biology and treatment, the clinical outcomes of MCC are still poor, suggesting that an individual prediction model is needed to facilitate better treatment stratification and outcome evaluation. However, to the best of our knowledge, there is no individual prognostic model for MCC owing to its rarity.

Currently, the most commonly used standard for prognostication in MCC is the American Joint Committee on Cancer (AJCC) staging system. However, an obvious shortcoming of AJCC staging system predicting survival was its low accuracy. Since other factors such as age, gender and site, are also associated with patients' outcome, a personalized predictive model for MCC patients is warranted.

A nomogram is a reliable tool to predict and quantify an individual probability of a certain clinical event by integrating prognostic and determinant factors, so that it could predict patient outcomes accurately and facilitate personalized medicine. Therefore, in current study, we sought to develop and validate a nomogram and built a risk stratification system for MCC patients based on a large set MCC dataset from the Surveillance, Epidemiology and End Results (SEER) database. Besides, we compared the predictive accuracy of the survival nomogram with that of the American Joint Committee on Cancer (AJCC) stage.

Patients And Methods

Cohort population

A retrospective study was conducted based on the information from the SEER database, a public available cancer statistics database, which is constitutive of 18 cancer registries in the United States and covers about 28% of the total population of the United States (https://seer.cancer.gov/data/). Informed consent was waived for the use of public data from the SEER.

The SEER*Stat software (Version 8.3.6) was used to recruit MCC patients from 2010 to 2015. All cases were diagnosed as MCC by histology confirmation with the International Classification of Diseases for Oncology, Third Edition (ICD-O-3) histologic codes 8247/3 (Merkel cell carcinoma). According to the Primary Site – labeled codes, primary sites were classified into four sites as follows: NOS/overlapping codes (C448-C449), head and neck (C440-C444), trunk (C445), extremities (C446-C447). We selected patients over 18 years of age and those with only one primary tumor. Patients with unknown staging or unknown follow-up were excluded. The patient screening flowchart was showed in **Supplemental figure 1**.

Patient demographics including age, gender, race, marital status, primary sites, tumor stage, treatment [primary site surgery, sentinel lymph node biopsy and/ or lymph nodes removal (SLNB and or LN

removel), chemotherapy and radiation] were obtained from the database. Tumor stage in SEER database between 2010 to 2015 was recorded according to the AJCC Cancer Staging Manual, 7th edition. The endpoint of our study was overall survival (OS), which was defined as the time from cancer diagnosis to the time of death from any cause or of the last follow-up.

Statistical Analyses and Nomogram Development

All included MCC patients were randomly assigned to the training and validation cohort in a ratio of 7:3 using the random sampling function in version 3.6.2 of R software. Patient characteristic between the training and validation cohort were compared by descriptive statistics. Categorized variables were analyzed by Chi-square tests and continuous variables were compared using the *t* test. Univariate and multivariate Cox models were performed to identify variables that significantly affect overall survival (OS) in the training cohort. Based on these prognostic factors in training cohort, we established a nomogram to predict the 3-year and 5-year OS rate for MCC patients with the “rms” package. The discrimination and calibration of the nomogram were validated in the training and validation cohort. To evaluate discriminative ability, concordance index (C-index) and area under curve (AUC) value were calculated. Typically, the C-index and AUC value greater than 0.7 suggested relatively favorable discrimination. Calibration ability was evaluated by calibration plots. The integrated discrimination improvement (IDI) and the net reclassification improvement (NRI) were calculated to compare the accuracy of the established nomogram with that of AJCC staging system. Decision curve analyses (DCA) were performed to assess the clinical usefulness and benefits of the nomogram. A risk stratification system was built according to the total points of each patient in training cohort. We classified all patients into the low-, intermediate-, and high-risk groups with a similar number of cases. Kaplan-Meier method were used to generate survival curves and the Log Rank test was performed to compare the differences among the curves. All statistical tests were two-sided and a P value < 0.05 was considered statistically significant. All statistical analyses were conducted using the statistical software packages R version 3.6.2 (http://www.R-project.org, The R Foundation) and SPSS statistics version 23.0 (IBM SPSS Statistics, New York, United States).

Results

Patient characteristics

A total of 1863 MCC patients from 2010 to 2015 were enrolled in our study, who were randomly divided into the training (n=1307) and validation (n=556) cohort by a ratio of 7:3. Patient characteristics were summarized in **Table 1**. The average age of MCC patients in the total, training, and validation cohorts were 73.92 years, 74.02 years and 73.70 years, respectively. In the total cohort, the majority of cases were male (n=1145, 61.5%) and white (n=1760, 94.5%). There were 41.9% (n=780) and 39.0% (n=726) MCC occurring in skin of extremities and skin of head and neck, respectively. Most patients (n=1567,84.1%) in the total cohort study received primary site surgery. 64.3% (n=1198) patients underwent SLNB and or LN removel and 55.7% (n=1037) patients were treated with radiation. However, only 13.5% (n=251) patients

underwent chemotherapies. Baseline characteristics between the training and validation cohort were balanced (all P>0.05).

Independent prognostic factors for OS in training cohort

The median follow-up time was 43.0 months (95% CI: 40.9-45.1 months) and the median OS was 59.0 months (95% CI: 51.6-66.4 months) in the training cohort. Univariate and multivariate Cox regression analysis were conducted to screen significant prognostic factors for OS in the training cohort. In the univariate analysis (**Table 2**), nine variables were significantly associated with OS, including age, gender, marital status, primary site, tumor stage, primary site surgery, SLNB and or LN removel, radiation and chemotherapy (all P <0.05). Then we performed multivariate analyses to identify factors identified in the univariate analyses. Age, gender, marital status, primary site, stage, SLNB and or LN removel, radiation were independent risk factors for prognosis of MCC patients (**Table 2**).

Development and validation of Nomogram

Based on all independent prognostic indicators for OS in the training cohort, we construct a prognostic model to predict 3- and 5- year OS for MCC patients. The prognostic model was virtually presented in the form of a nomogram **(Figure 1)** and was validated using a dependent validation cohort. A C-index and ROC curves were used to evaluate the discrimination performance. The C-index of OS prediction was 0.744 (95% CI: 0.722-0.766) in the training set and 0.737 (95% CI: 0.706-0.768) in the validation set. The ROC curves **(Figure 2)** showed that the AUC values for predicting 3- and 5-year OS were over 0.75 in the both training and validation cohorts. The calibration curves (**Supplemental figure 2**) showed optimal consistencies between the predicted and observed survival probability in the both training and validation cohorts. Overall, our nomogram had good discrimination and calibration ability and was validated in the validation cohort.

Comparison of clinical value between nomogram and the 7th AJCC TNM stage system

AJCC tumor stage system was traditionally used to predict prognosis stratification for MCC patients in clinical practice. As tumor stage in SEER database between 2010 to 2015 was recorded according to the AJCC Cancer Staging Manual, 7th edition, we sought to evaluate whether the nomogram that included the7th AJCC TNM stage information and other prognostic factors could perform better than 7th AJCC TNM stage system alone in stratifying OS. Firstly, the C-index for OS prognosis by the nomogram was 0.744, which was significantly higher than the C-index of 0.659 for OS prognosis by the 7th AJCC tumor stage alone, suggesting that our nomogram had better accuracy in predicting OS for MCC patients in training cohort. And the result was also confirmed in the validation cohort. We further calculate NRI and IDI value to evaluate the accuracy between the established nomogram and the 7th AJCC TNM stage alone **(Table 3)**. The NRI for 3-year and 5-year OS were 0.327 (95% CI: 0.269-0.399, P<0.001), 0.43 (95% CI: 0.341-0.503, P<0.001) and the IDI value for 3-year and 5-year OS were 0.119, (95% CI: 0.081-0.159, P<0.001), 0.164, (95% CI: 0.121 -0.202), respectively. These results were also observed in the validation

cohort (P<0.001), illustrating that the nomogram could predict patient survival more accurately compared to the 7th AJCC TNM stage alone.

The decision curve analysis was performed to compare the clinical benefits among the nomogram and the 7th AJCC TNM stage system (**Figure 3)**. The decision curves displayed that if the threshold probability of a patient is > 15%, the established nomogram in prognosticating OS yielded more benefit than that of than all patients dead scheme or none patient dead scheme in the both training and validation cohorts. Moreover, in this range, the nomogram could better predict the 3- and 5-year OS than the 7th AJCC TNM stage system, as it added more net benefits compared with the 7th AJCC TNM stage system.

Risk stratification based on the nomogram

A risk stratification system was built based on the total points of each patient in the training cohort. MCC patients were classified into three risk groups: the low-risk group (total points ≤ 96), the intermediate-risk group (96<total points ≤132) and the high-risk group (total points >132). As the **(Supplemental figure 3A-C)** showed, the 7th AJCC tumor stage system was relatively unsatisfactory in stratifying MCC patients between stages II and III in the training, validation cohorts and whole population. However, OS in three risk groups was accurately differentiated in the training cohort, validation cohort and whole population **(Supplemental figure 3 D-F)**. These results suggested that the risk stratification system could perfectly classified patients into three risk groups and showedgreater discrimination than he 7th AJCC tumor stage system.

Discussion

MCC was a rare but highly malignant tumor, until now its prognosis and treatment treatment decision were mainly based on the conventional TNM stage system. However, it is well known that the stage system only takes the anatomical extent of the disease into consideration and not think about patient clinicopathological characteristics and treatment which also affected patient prognosis, so that the TNM stage system was unable to completely reflect the accurate prognosis and personal feature. Nomograms for some cancers have been established and shown to be more accurate than the conventional staging systems for predicting survival[24-28]. Nomogram for MCC was not yet established. Therefore, in current study, we established a nomogram for MCC patients based on the data from SEER database, which included eight significant prognostic factors that were selected by univariate and multivariate Cox analysis. According to the standard deviation along nomogram scales, we could intuitively find that the 7th AJCC TNM stage was the most important factor, followed by SLNB and or LN removal, age, radiation, gender, marital status and primary site.

In fact, some important prognostic factors for MCC patients, including age, gender, marital status and primary site, have been proposed in existing literatures. Importantly, in current study, we fully took these factors into consideration and incorporated them into the nomogram. For example, a large population study of 6908 MCC patients reported that age, gender, primary site and marital status were important

factors affecting mortality of MCC[29]. Similarly, a study of 3048 MCC patients reported that age older than 75 years and male sex showed negative effect on OS[30]. Moses Tam et al. also demonstrated that women with MCC showed improved survival compared to man with MCC, even after propensity score-matched analysis[31]. Some studies thought the underlying cause is because women have stronger innate and adaptive immune responses than men[32,33]. These results consistent with our study suggested that demographic and clinicopathological characteristics of MCC patients were strongly associated with OS. When predicting personal prognosis, these factors should be considered.

Patient treatments were another important prognostic factors. In present study, undergoing SLNB and or LN removal was associated with improved OS. It is well known that lymph node invasion was the major route of metastasis in MCC and patients with lymph node metastasis have accelerated disease progression, associated with worse survival[34,35]. SLNB and or LN removal was a valuable tool to assess the regional LN status. SLNB is recommended for patients with clinically negative lymph nodes, which has been shown to improve survival(30). Well, LN removal was an important treatment for patients with clinically positive lymph nodes or SLNB-positive and it also could quantify regional metastatic lymph nodes and assess exact node stage. A recent population study showed that number of metastatic LNs was the dominant nodal factor for survival in patients with MCC[36]. Therefore, SLNB and or LN removal was a strong favorable predictor for OS in patients with MCC as it permitted more accurate staging and more appropriate prognosis and management.

Besides, receiving radiotherapy was also a significant favorable prognostic factor. Previous study has shown that MCC is very responsive to radiotherapy, which could control the local disease in 75–85% of cases[37-40]. Radiotherapy has been used as the definitive, adjuvant, and palliative treatment of patients with MCC within a multidisciplinary framework, which was highly effective in providing locoregional control benefits in many literatures[41]. Local control may further translate into survival benefits. Therefore, receiving radiotherapy as an effective treatment for MCC showed positive effect on survival.

Chemotherapy was not associated with improved OS and it was a negative factor for OS in univariate cox analysis in present study. This was because patients with chemotherapy in our study had a higher rate of adverse prognostic features, such as stage III-IV disease (stage III: 59.3% vs 31.9%, stage IV: 34.1% vs 5.6%, P<0.001), male sex (68.2% vs 60.4%, P=0.027), and extremities primary (26.9% vs 5.9%, P<0.001), compared with patients without chemotherapy (**Supplemental Table 1**). These adverse prognostic features may be responsible for worse prognosis in patients with chemotherapy rather than chemotherapy itself. Besides, only 182 (13.9%) patients in the training cohort underwent chemotherapy, which made it difficult to evaluate its role correctly. And it is noticed that chemotherapy for MCC patients showed short duration of response with the reported median progression-free survival of 61 days and 94 days in two studies, as well as, high rates of toxic death[42-44].

Notably, primary site surgery was an important component for MCC, however it was not included in the nomogram. This might be because in present study most patients (84.1%) had undergone surgery,

making its effects hard to be analyzed properly. In addition, the management of surgery, including its extent and margins, should be decided on an individual basis and these surgery related factors were not discussed in detail in our study. In fact, wide local excision of the primary tumor is the standard of care and a 1–2 cm excision margin down to the muscle fascia or the pericranium was recommended in guideline[19]. Therefore, we could not be interpreted as meaning that surgery has no benefit on survival.

Overall, in current study, we established a prognostic nomogram for MCC patients, which integrates demographic and clinicopathological characteristics, patient treatment. The nomogram performed well in predicting overall survival, with good discrimination (C-index, 0.744; AUC>0.75) and calibration in the primary cohort and was validated in the validation cohort (C-index, 0.737; AUC>0.80). When compared with the conventional TNM stage, our nomogram had increased accuracy for predicting OS, reflecting by that the C-index of nomogram was 0744 greater than 0.659 for the conventional TNM stage. Besides, the positive NRI and IDI of the nomogram versus the staging system further suggested that the nomogram could predict survival more accurately than the conventional TNM stage alone. Furthermore, DCA curves showed that the established nomogram predicted survival with better clinical benefit and utility compared with the conventional staging system. Moreover, patients were classified into low-, intermediate-, and high-risk groups according to their nomogram total points. The Kaplan-Meier curves clearly showed significant differences in OS among the three risk groups with better discrimination than the conventional TNM stage. Overall, our nomogram was a valuable tool to assist clinicians in predicting prognosis of MCC patients and facilitate personalized medicine.

However, there are some limitations in present study. Firstly, we were unable to evaluate the prognostic role of immunity therapy and surgical margins in MCC due to the retrospective nature and limited data availability of SEER database. Besides, it would be better if there was a multicenter clinical validation cohort to evaluate the external utility of the nomogram. However, as MCC is very rare, it is difficult for us to collect a multicenter clinical validation. But in current study we evaluated a large set of samples including the data from 18 medical centers registered in the SEER database, which represent the populations of different areas.

Conclusion

In conclusion, our nomogram had better accuracy, better clinical utility, and more precise prognosis prediction than the conventional staging system, which may be a valuable tool for predicting survival of patients with MCC.

Abbreviations

MCC:Merkel cell carcinoma

OS:Overall survival

SEER:Surveillance, Epidemiology and End Results

AUC:Area under receiver operating characteristic curve

DCA:Decision curve analysis

NRI:Net reclassification index

IDI:Integrated discrimination improvement

MCPyV:Merkel cell polyomavirus

AJCC:American Joint Committee on Cancer

SLNB:Sentinel lymph node biopsy

LN:Lymph nodes

C-index:Concordance index

Declarations

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Contributions

MW and YQ designed this study; FT, YXL, YL, XLW, SYL, LH, BYZ, and WJL collected the data; MW and YQ were responsible for the statistical analysis;MW wrote the draft; YCW revised this draft; All authors read and approved the final manuscript.

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Ethics Declarations

Ethics approval and consent to participate

Approval was waived by the local ethics committee, as SEER data is publicly available and de-identified.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Tables

Table 1: Clinical characteristics and treatment information of MCC patients

Characteristic	Whole population, No. (%) (n = 1863)	Training cohort, No. (%) (n = 1307)	Validation cohort, No. (%) (n = 556)	p value
Age, y, mean (SD)	73.92 (11.64)	74.02 (11.53)	73.70 (11.89)	0.581
Age				0.678
≤75	967 (51.9)	683 (52.2)	284 (51.1)	
>75	896 (48.1)	624 (47.7)	272 (48.9)	
Gender				1.000
Female	718 (39.5)	504 (38.6)	214 (38.5)	
Male	1145 (61.5)	803 (61.4)	342 (61.5)	
Race				0.202
Non-white	103 (5.5)	66 (5.0)	37 (6.7)	
White	1760 (94.5)	1241 (95.0)	519 (93.3)	
Marital status				0.733
Non-married	760 (40.8)	537 (41.1)	223 (40.1)	
Married	1103 (59.2)	770 (58.9)	333 (59.9)	
Primary site				0.173
Skin, NOS	169 (9.1)	115 (8.8)	54 (9.7)	
Head and neck	726 (39.0)	492 (37.6)	234 (42.1)	
Trunk	188 (10.1)	132 (10.1)	56 (10.1)	
Extremities	780 (41.9)	568 (43.5)	212 (38.1)	
AJCC Stage				0.125
I	723 (38.8)	487 (37.3)	236 (42.4)	
II	321 (17.2)	228 (17.4)	93 (16.7)	
III	638 (34.2)	467 (35.7)	171 (30.8)	
IV	181 (9.7)	125 (9.6)	56 (10.1)	
Surgery				0.965
NO	292 (15.7)	206 (15.8)	86 (15.5)	
YES	1567 (84.1)	1098 (84.0)	469 (84.4)	
Unknown	4 (0.2)	3 (0.2)	1 (0.2)	

SLNB and/or LN removal				0.408
NO	642 (34.5)	447 (34.2)	195 (35.1)	
YES	1198 (64.3)	841 (64.3)	357 (64.2)	
Unknown	23 (1.2)	19 (1.5)	4 (0.7)	
Radiation				0.692
NO	796 (42.7)	557 (42.6)	239 (43.0)	
YES	1037 (55.7)	731 (55.9)	306 (55.0)	
Unknown	30 (1.6)	19 (1.5)	11 (2.0)	
Chemotherapy				0.422
NO	1612 (86.5)	1125 (86.1)	487 (87.6)	
YES	251 (13.5)	182 (13.9)	69 (12.4)	

Note: MCC, Merkel cell carcinoma; NOS, not otherwise specified; SLNB, sentinel lymph node biopsy, LN, lymph node;

Table 2 Univariate and multivariate analyses of prognostic factors of overall survival in MCC patients

Factors	HR (95% CI)	p value	HR (95% CI)	p value
Age, (years)				
>75 vs ≤75	2.14 (1.80-2.54)	**<0.001**	2.12 (1.76-2.54)	**<0.001**
Gender				
Male vs Female	1.31 (1.10-1.56)	**0.002**	1.42 (1.18-1.71)	**<0.001**
Race				
White vs non-white	1.14 (0.75-1.73)	0.532	-	-
Marital status				
Married vs non-married	0.67 (0.57-0.79)	**<0.001**	0.71 (0.60-0.85)	**<0.001**
Primary site				
Trunk vs head and neck	1.03 (0.78-1.36)	0.815	1.00 (0.75 - 1.34)	0.993
Upper and lower extremities vs head and neck	0.71 (0.59-0.86)	**<0.001**	0.85 (0.70-1.04)	0.109
Skin, NOS vs head and neck	1.19 (0.89-1.57)	0.223	0.65 (0.45-0.95)	**0.024**
AJCC stage				
II vs I	1.52 (1.16-1.99)	**<0.001**	1.65 (1.25-2.18)	**<0.001**
III vs I	2.09 (1.69-2.58)	**<0.001**	3.64 (2.80-4.71)	**<0.001**
IV vs I	7.53 (5.81-9.77)	**<0.001**	7.44 (5.44-10.17)	**<0.001**
Primary site surgery				
Yes vs No	0.87 (0.41-0.62)	**<0.001**	0.87 (0.65-1.16)	0.342
Unknown vs No	0.99 (0.25-4.03)	0.996	1.27 (0.30-5.33)	0.746
SLNB and/or LN removal				
Yes vs No	0.45 (0.38-0.53)	**<0.001**	0.47 (0.37-0.58)	**<0.001**

Unknown vs No	0.76 (0.39-1.47)	0.415	0.66 (0.33-1.30)	0.229
Radiation				
Yes vs No	0.75 (0.63-0.89)	**<0.001**	0.67 (0.57-0.80)	**<0.001**
Unknown vs No	0.63 (0.28-1.41)	0.262	0.54 (0.24-1.22)	0.137
Chemotherapy				
Yes vs No	2.01 (1.64-2.47)	**<0.001**	1.21 (0.94-1.55)	0.135

Note: HR, hazard ratio; CI, Confidence interval; NOS, not otherwise specified;

SLNB, sentinel lymph node biopsy; LN, lymph node;

Table 3: NRI and IDI of the nomogram and the 7th AJCC staging system alone in predicting 3-year and 5-year survival for MCC patients

Index	Training cohort			Validation cohort		
	Estimate	95% CI	P value	Estimate	95% CI	P value
NRI (The nomogram vs The AJCC staging system)						
3-year OS	0.327	(0.269-0.399)	**<0.001**	0.328	(0.223-0.414)	**<0.001**
5-year OS	0.436	(0.341-0.503)	**<0.001**	0.356	(0.218 -0.480)	**<0.001**
IDI (The nomogram vs The AJCC staging system)						
3-year OS	0.119	(0.081-0.159)	**<0.001**	0.124	(0.082-0.175)	**<0.001**
5-year OS	0.164	(0.121 -0.202)	**<0.001**	0.142	(0.087-0.214)	**<0.001**

Note. NRI: net reclassification improvement; IDI: integrated discrimination improvement; AJCC: American Joint Committee on Cancer; MCC: merkel cell carcinoma; OS: overall survival; CI: confidence interval;

Figures

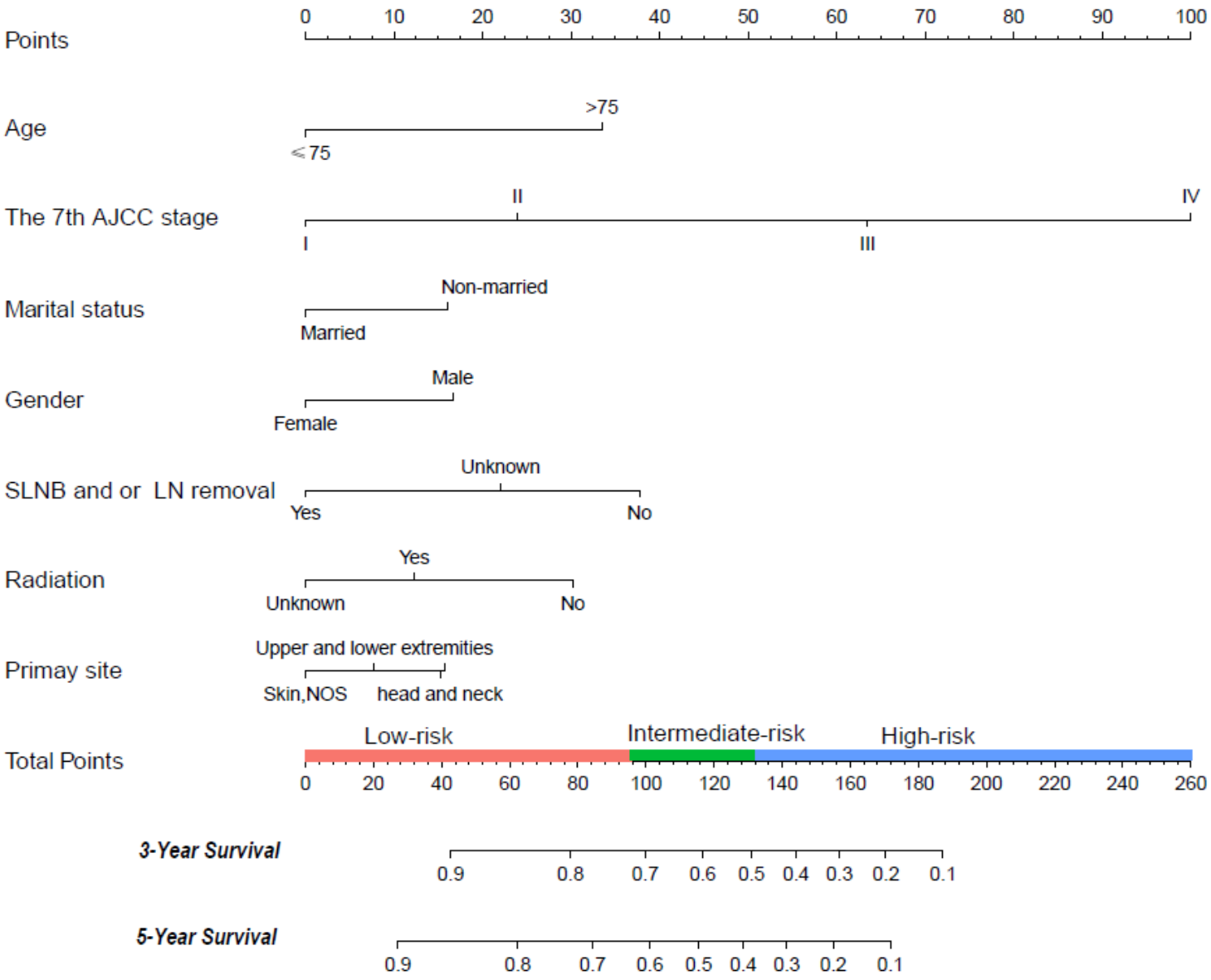

Figure 1

Survival nomogram for MCC patients; Prediction of 3-year and 5-year OS in MCC patients and the risk groups based on the total points of each patients in training cohort; MCC, Merkel cell carcinoma, OS: overall survival.

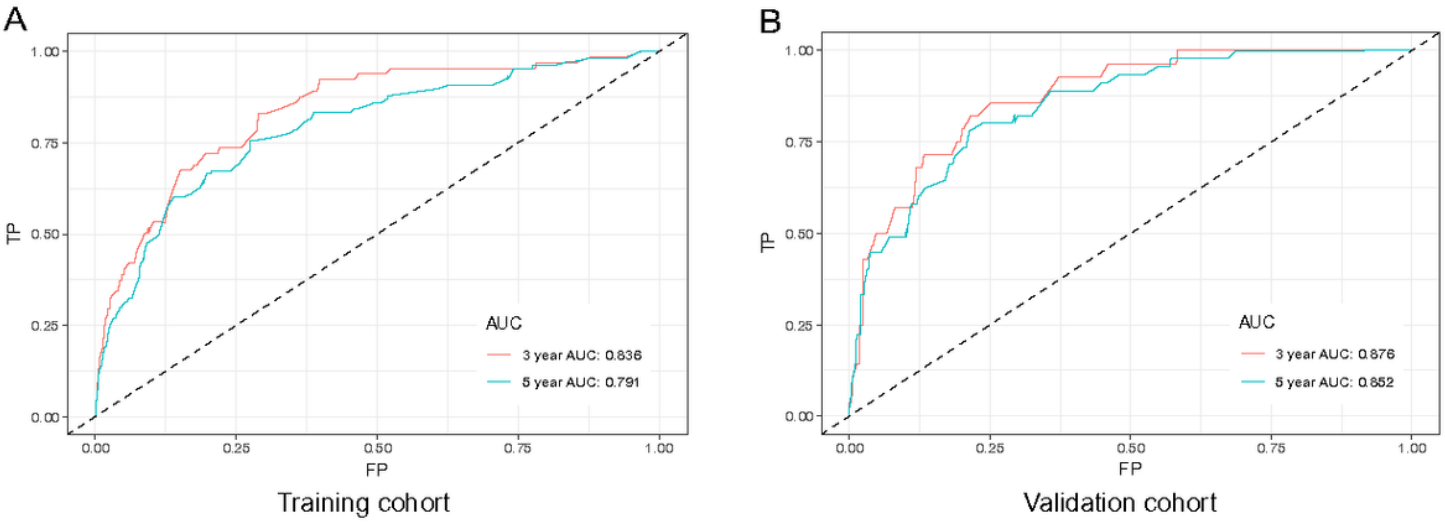

Figure 2

ROC curves depicting predictive performance and discrimination of the survival nomogram; ROC curves for 3-year and 5-year OS of MCC patients in (A) the training cohort and (B) the validation cohort; ROC: receiver-operating characteristic; OS: overall survival; MCC, Merkel cell carcinoma, FP: false positive; TP: true positive.

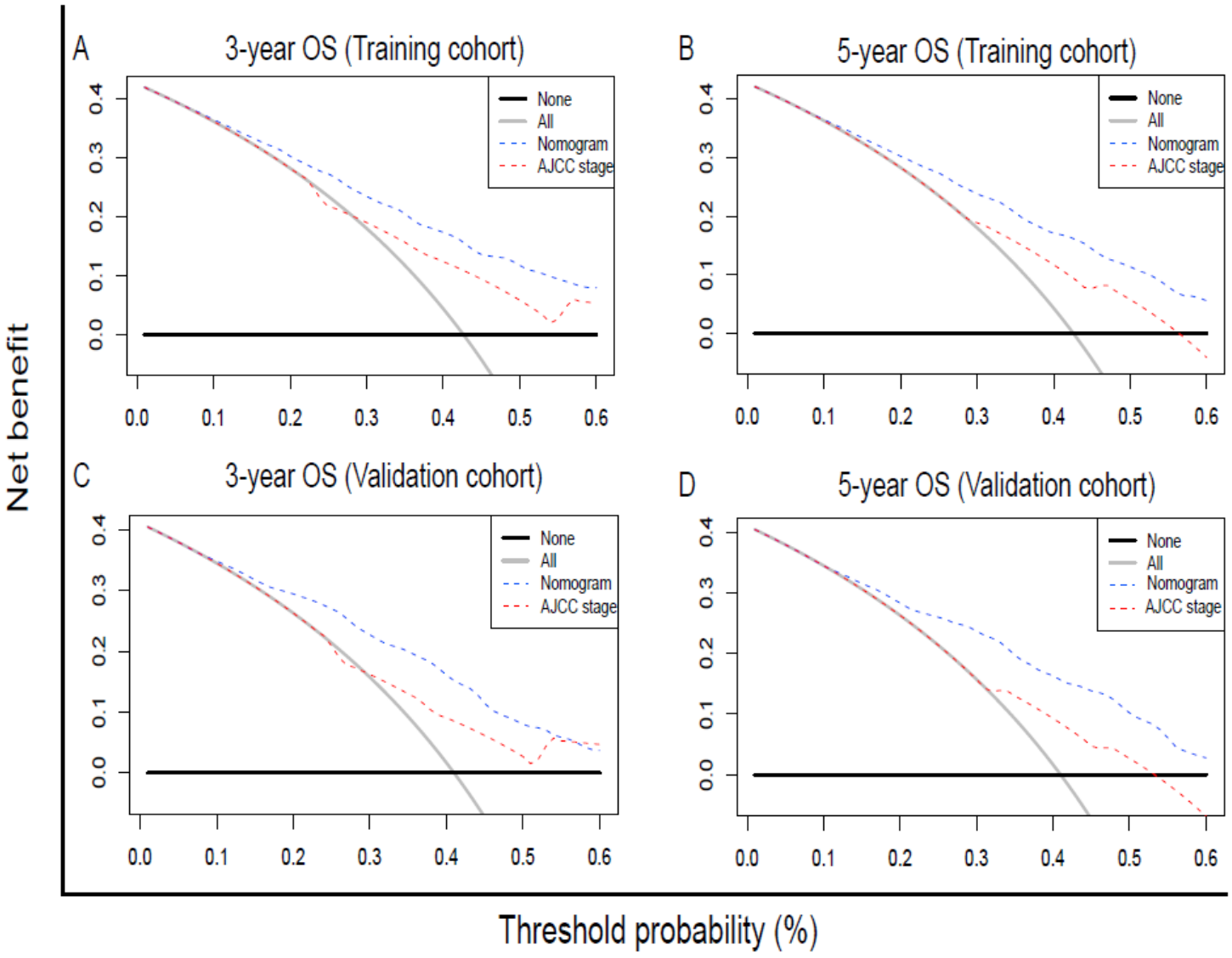

Figure 3

Decision curve analysis for the nomogram and AJCC stage in prediction of prognosis of MCC patients at 3-year and 5-year OS in the training (A-B) and validation cohorts (C-D). OS: overall survival; MCC, Merkel cell carcinoma.

Supplementary Files

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

- SupplementalTable1.docx
- supplementfigure1.pdf
- supplementfigure2.pdf
- supplementfigure3.pdf