European Review for Medical and Pharmacological Sciences 2022; 26: 9437-9446

Development of a prognostic prediction model for patients with cutaneous malignant melanoma: a study based on the SEER database

X.-Y. HE[1], Y.-F. GAO[2], Y.-P. HUANG[1], X.-W. ZOU[1], D. WANG[1], H. SU[1]

[1]Department of Dermatology, Chengdu First People's Hospital, Chengdu, Sichuan, China
[2]Department of Urology, Chengdu Second People's Hospital, Chengdu, Sichuan, China

Xueyang He and Yunfeng Gao equally contributed to this work

Abstract. – OBJECTIVE: To investigate the prognostic factors of cutaneous malignant melanoma (CMM) and establish an effective nomogram survival prediction model.

PATIENTS AND METHODS: The clinical data of patients diagnosed with stage M0 CMM from 2000 to 2019 in the Surveillance, Epidemiology, and End Results (SEER) database were collected and retrospectively analyzed. The variables that may be related to prognosis were analyzed by Lasso-Cox regression analysis using R software. Independent prognostic factors were screened. A nomogram model for predicting the prognosis of CMMC was drawn, and its accuracy was verified by c-index, NR, IDI and calibration curve.

RESULTS: A total of 2,679 patients with CMM were included. Lasso-Cox analysis showed that male sex, multiple tumors, higher T stage, SEER stage, widowed, divorced, and separated often indicated poor prognosis. The nomogram model calibration curve was in good agreement with the ideal curve, and the C-index was 0.734 in the training group and 0.761 in the validation group, respectively. In the training group, the AUC of 1-, 3-, 5- and 8-year survival were 0.80, 0.75, 0.74 and 0.72, respectively. In the validation group, the AUC of 1-, 3-, 5- and 8-year survival were 0.75, 0.79, 0.78 and 0.79, respectively. NRI and IDI were superior to the prediction ability of TNM stage and SEER stage ($p < 0.05$). The established prognostic score can divide patients into high and low score groups with significant prognostic difference ($p < 0.05$).

CONCLUSIONS: Sex, SEER stage, T stage, total number of tumors and marital status are independent prognostic factors for CMM patients, and the nomogram model presented a better performance than TNM stage and SEER stage in predicting the prognosis of CMM patients.

Key Words:
Cutaneous malignant melanoma, Nomogram, SEER, Prognostic, Lasso-Cox.

Introduction

Malignant melanoma (MM) is a fatal malignant tumor. Primary MMs are more common in the skin and mucous membranes, and a few can also occur in the eyes, digestive tract and other tissues and organs[1]. Cutaneous malignant melanoma (CMM) is a malignant melanoma primarily located in the skin, which accounts for 1-3% of all MM[2]. The incidence of CMM has been increasing in recent years[3]. CMM is a highly invasive skin malignant tumor, which can metastasize to almost any tissue in the body[4]. Its malignant degree and mortality rate rank first among skin malignant tumors[5]. The pathogenesis of CMM is unknown. Big data studies[6,7] showed that the most important risk factor for the disease was excessive exposure to ultraviolet rays. Data[8] from the United States in 2018 showed that age, race, and gender were independent risk factors for malignant melanoma. The metastasis of CMM occurs early with high mortality, in patients with advanced malignant melanoma with a 5-year survival rate lower than 20%[9]. Traditional TNM staging and SEER stage have certain prognostic ability, but they have inherent defects, because they only rely on anatomical indicators and lack of multidisciplinary comprehensive metrics[10]. According to previous studies[11-14], the following factors may also affect the prognosis of CMM patients: gender[11], age[12], tumor size[13], surgery[14], etc. Clinical prognostic models incorporating multiple prognostic factors will more accurately assess cancer prognosis; however, there is a lack of prognostic analysis of CMM patients based on large sample size.

Surveillance, Epidemiology and End Results (SEER) database can provide the incidence of

Corresponding Author: Hong Su, MD; e-mail: shscpf@163.com

cancer, survival rate and mortality data[15]. This study used CMM patients from SEER databases for screening its influence factors of prognosis, and then a prognostic score was constructed to individualize the relevant prognosis of patients.

Patients and Methods

Study Population

Data were extracted from SEER database. The database is jointly established by 18 registries in various states and regions of the United States. It covers a wide range of populations and can provide large samples of data for clinical research. SEER* Stat software version 8.4.0 (available at: https://seer.cancer.gov/seerstat/) was used to collect data. The inclusion criteria were: (1) Pathological diagnosis of malignant melanoma; (2) The diagnosis time was between January 2010 and December 2019. From January 2010 to December 2019, a total of 33,694 patients were pathologically diagnosed as malignant melanoma. Exclusion criteria: (1) patients diagnosed only based on autopsy or death certificate; (2) The 7th edition of TMN staging was diagnosed as M1; (3) Unknown surgical procedure; (4) Survival time less than 1 month; (5) The following information was unknown, including gender, age, race, tumor location, tumor laterality, tumor size, number of primary tumors, marital status, income, surgery, radiotherapy, chemotherapy, systemic therapy, SEER stage, the 7th edition of TMN staging. A total of 2,679 patients were included in the final cohort. According to the current international practice, the training group and validation group were commonly divided into 7:3. In this study, all patients were divided into training group (1,876 cases) and validation group (803 cases) according to the ratio of 7:3 by random number table method. The basic clinical characteristics of the patients are shown in Table I.

Research Variables

Patients pathologically diagnosed with CMM from January 2010 to December 2019 were collected through the SEER database. Patients were screened according to the inclusion and exclusion criteria. The following information was collected: year of diagnosis, gender, age, race, primary site, laterality, tumor size, total number of *in situ*/malignant tumors, marital status, median household income, surgery, radiotherapy, chemotherapy, systemic therapy, SEER stage, 7th TMN stage, survival time and survival status. The operation was divided into no operation, local resection of the primary lesion, and extended resection. Marital status was categorized as married, unmarried, and other (widowed, divorced, separated, and domestic partner). All cases were randomly divided into training group and validation group according to the ratio of 7:3. Lasso-Cox regression analysis was used to obtain the prognostic factors, and the final selected prognostic factors were used to establish the clinical prediction model, and the model was validated in the validation group.

Statistical Analysis

Lasso-Cox regression analysis was used to assess independent prognostic factors associated with survival. Lasso regression was used to screen prognostic factors, and then the screened variables were included in multivariate Cox analysis. Variables with $p < 0.05$ were used to construct a nomogram to form a new clinical prediction model. Finally, sex, site of tumor, SEER stage, T stage, total number of tumors and marital status were included in the prognosis analysis. The bootstrap method was used to verify the model internally. The self-sampling times B=1,000, the discrimination of the model was evaluated by C-index and area under curve (AUC), and the consistency of the model was evaluated by calibration diagram. The closer the C-index is to 1, the more reliable the model is. Receiver operating characteristic (ROC) curves, time-dependent ROC curves, and the AUC were derived using the "pROC" and the "timeROC" packages (R Foundation for Statistical Computing, Vienna, Austria) respectively. The closer the calibration curve is to the 45° diagonal, the better the prediction ability of the nomogram. Finally, the prediction ability of the new model was compared with the 7th TNM staging system and SEER stage, the integrated discrimination improvement (IDI), and net reclassification improvement (NRI) values were calculated, and the decision curve analysis (DCA) was drawn. The "Survminer" package (R Foundation for Statistical Computing, Vienna, Austria) was used to select the best cutoff for prognosis score, and patients in the training group and validation group were divided into high-risk group and low-risk group, respectively. The 1-, 3-, 5-, 8-year survival of patients in

Table I. Clinical characteristics of the training cohort and the test cohort.

	Level	Overall	Train	Test	p
N		2679	1876	803	
Sex (%)	Male	1656 (61.8)	1169 (62.3)	487 (60.6)	0.435
	Female	1023 (38.2)	707 (37.7)	316 (39.4)	
Year of diagnosis (%)	2010	375 (14.0)	255 (13.6)	120 (14.9)	0.768
	2011	381 (14.2)	263 (14.0)	118 (14.7)	
	2012	437 (16.3)	315 (16.8)	122 (15.2)	
	2013	531 (19.8)	379 (20.2)	152 (18.9)	
	2014	538 (20.1)	371 (19.8)	167 (20.8)	
	2015	417 (15.6)	293 (15.6)	124 (15.4)	
Site (%)	C44.5-Skin of trunk	905 (33.8)	633 (33.7)	272 (33.9)	0.16
	C44.6-Skin of upper limb and shoulder	699 (26.1)	500 (26.7)	199 (24.8)	
	C44.7-Skin of lower limb and hip	479 (17.9)	338 (18.0)	141 (17.6)	
	C44.3-Skin other/unspec parts of face	493 (18.4)	326 (17.4)	167 (20.8)	
	C44.2-External ear	103 (3.8)	79 (4.2)	24 (3.0)	
Laterality (%)	Left - origin of primary	1215 (45.4)	846 (45.1)	369 (46.0)	0.917
	Right - origin of primary	1097 (40.9)	771 (41.1)	326 (40.6)	
	Not a paired site	367 (13.7)	259 (13.8)	108 (13.4)	
Seer stage (%)	Localized only	2442 (91.2)	1721 (91.7)	721 (89.8)	0.234
	Regional by direct extension only	219 (8.2)	144 (7.7)	75 (9.3)	
	Distant site(s)/node(s) involved	18 (0.7)	11 (0.6)	7 (0.9)	
7th Stage (%)	I	2166 (80.9)	1534 (81.8)	632 (78.7)	0.161
	II	336 (12.5)	226 (12.0)	110 (13.7)	
	III	177 (6.6)	116 (6.2)	61 (7.6)	
T (%)	T1	1897 (70.8)	1331 (70.9)	566 (70.5)	0.142
	T2	392 (14.6)	287 (15.3)	105 (13.1)	
	T3	216 (8.1)	139 (7.4)	77 (9.6)	
	T4	174 (6.5)	119 (6.3)	55 (6.8)	
N (%)	N0	2502 (93.4)	1760 (93.8)	742 (92.4)	0.176
	N1-3	177 (6.6)	116 (6.2)	61 (7.6)	
Chemotherapy (%)	YES	2653 (99.0)	1858 (99.0)	795 (99.0)	1
	NO	26 (1.0)	18 (1.0)	8 (1.0)	
Systemic (%)	YES	2592 (96.8)	1816 (96.8)	exact	0.813
	NO	87 (3.2)	60 (3.2)	27 (3.4)	
Number (%)	1	1511 (56.4)	1050 (56.0)	461 (57.4)	0.497
	> 1	1168 (43.6)	826 (44.0)	342 (42.6)	
Race (%)	White	2629 (98.1)	1844 (98.3)	514 (64.0)	0.352
	Other	50 (1.9)	32 (1.7)	18 (2.2)	
Marital (%)	Married (including common law)	1734 (64.7)	1220 (65.0)	514 (64.0)	0.693
	Single (never married)	503 (18.8)	354 (18.9)	149 (18.6)	
	Widowed or Divorced or Separated	442 (16.5)	302 (16.1)	140 (17.4)	
Income (%)	< $75,000	598 (22.3)	431 (23.0)	167 (20.8)	0.224
	≥ $75,000	2081 (77.7)	1445 (77.0)	636 (79.2)	
Surgery (%)	NO	23 (0.9)	18 (1.0)	5 (0.6)	0.416
	Local resection	1906 (71.1)	1322 (70.5)	584 (72.7)	
	Extended resection	750 (28.0)	536 (28.6)	214 (26.7)	
Radiation (%)	YES	2648 (98.8)	1859 (99.1)	789 (98.3)	0.075
	NO	31 (1.2)	17 (0.9)	14 (1.7)	
Size (median [IQR])	10.00 [6.00, 15.00]	10.00 [6.00, 15.00]	10.00 [6.00, 15.00]	0.03	
Age (median [IQR])	65.00 [53.00, 76.00]	65.00 [53.00, 76.00]	65.00 [53.00, 76.00]	0.028	
OS (%)	0	2084 (77.8)	1481 (78.9)	603(75.1)	0.029
	1	595 (22.2)	395 (21.1)	200 (24.9)	
Survival months (median [IQR])	70.00 [53.50, 89.00]	71.00 [54.00, 89.00]	70.00 [53.50, 89.00]	0.114	

the two groups were evaluated, Log-rank tests were utilized to identify the significance of differences in survival curves. All statistical p-values are two-side and $p < 0.05$ represents statistical significance.

Results

Basic Characteristics of The Study Cohort

Among the 2,679 patients, the median age was 65 (53-76) years, most of the patients were male

(61.8%), the most common site of cancer was skin of trunk (33.8%), and the occurrence probability of left and right sides was basically the same (45.4% *vs.* 40.9%). Single tumor accounted for 56.4%, married (64.7), $75,000+ income accounted for the majority (77.7%), most patients received local resection (71.1%), radiotherapy (98.8%), chemotherapy (99.0%). The median tumor size was 10 (6-15 mm), and the median survival time was 70 (53-89) months. The data are shown in Table I.

Variable Selection

Possible prognostic factors were explored using Lasso and multivariate Cox regression (Figure 1A and B). Lasso's one-fold standard error results showed that male sex, multiple tumors, higher T stage, SEER stage, widowed, divorced, and separated often indicated poor prognosis, and trunk tumors were better than limbs, head, face and neck and other parts on the prognosis. Other factors are not included in this model.

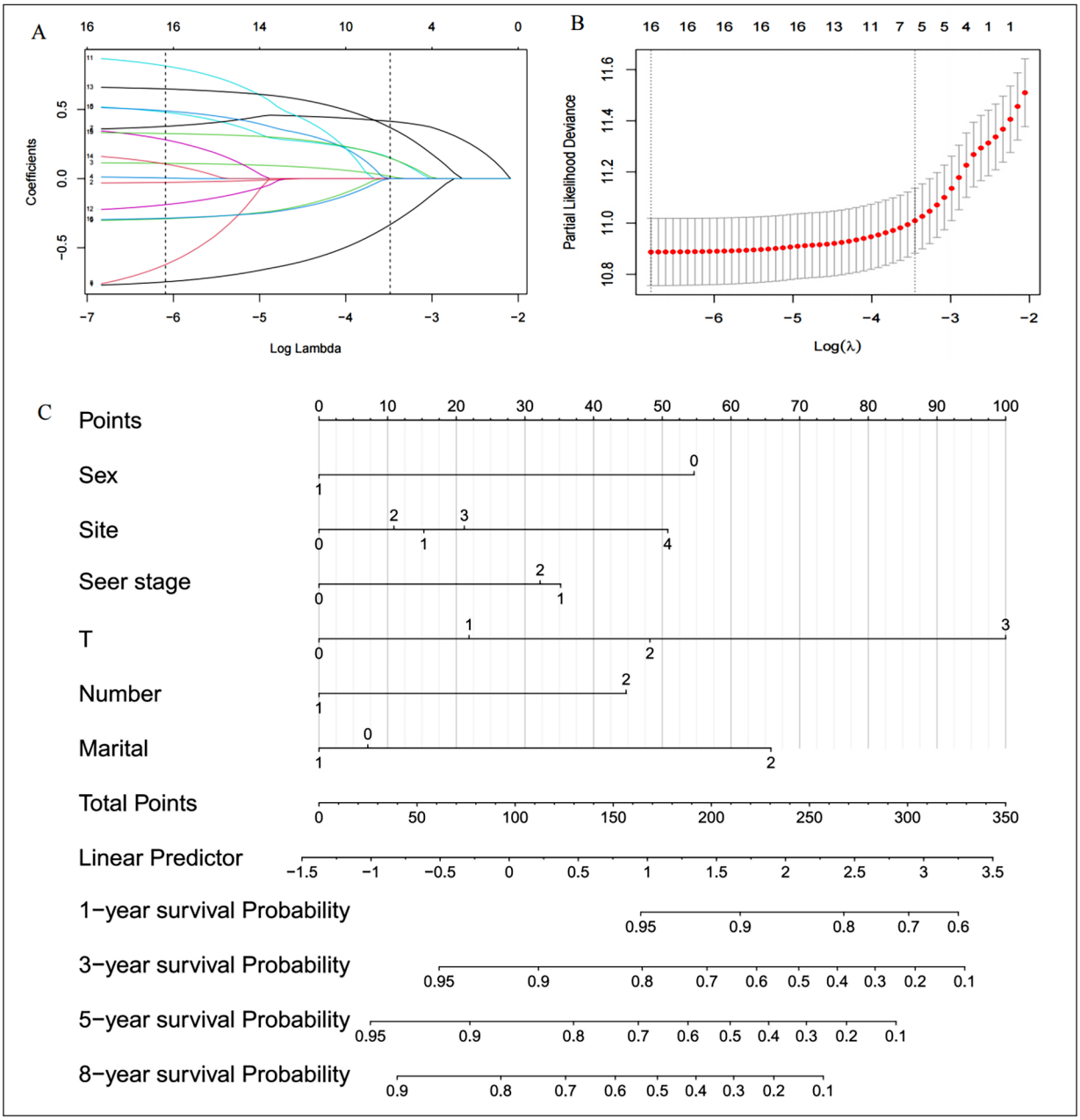

Figure 1. A-B, The lasso regression for the prognostic factors in panel; **C**, The nomogram in the panel.

Construction of Model

Six variables were included in the nomogram to predict the survival of cohorts 1-, 3-, 5-, and 8- survival (Figure 1C). According to the nomogram, T stage contributed the most to the prognosis, followed by marital status, gender, tumor location, tumor number and SEER stage. Each variable has a corresponding score on the score scale. By summing the scores and positioning on the total score table, the 1-, 3-, 5- and 8-year survival rates of malignant melanoma patients without metastasis could be predicted.

Accuracy Evaluation of the Model

The performance of C-index in the nomogram of the modeling group was significantly higher than that of the 7th TNM staging in the training group, the C-index of the nomogram was 0.734 [95% confidence interval (CI), 0.709-0.759], and the C-index of TNM staging was 0.635 (95% CI, 0.576-0.694). The C-index of SEER stage was 0.558 (95% CI, 0.538-0.578); Compared with TNM stage, the NRI of 1-, 3-, 5- and 8-year of the model were 0.053, 0.164 and 0.305, respectively. Compared with SEER stage, the 1-, 3-, 5- and 8-year NRI of the model are 0.432, 0.265, 0.426, 0.525 and 0.658, respectively. In the validation group, the C-index of nomogram was 0.761, 95% CI, 0.728-0.794, the C-index of TNM stage was 0.617 (95% CI, 0.578-0.656), and the C-index of SEER stage was 0.548 (95% CI, 0.521-0.575). Compared with TNM stage, the NRI of 1-, 3-, 5- and 8-year models were 0.263, 0.390, 0.475 and 0.672, respectively. Compared with SEER stage, the 1-, 3-, 5- and 8-year NRI of the model are 0.223, 0.632, 0.708 and 0.792, respectively. In both the training group and the validation group, the IDI of our model was better than that of TNM stage or SEER stage, and the difference was statistically significant ($p < 0.05$). In the training group, the AUC of 1-, 3-, 5- and 8-year nomogram were 0.80, 0.75, 0.74 and 0.72, respectively, in the validation group, the AUC of 1-, 3-, 5- and 8-year nomogram were 0.75, 0.79, 0.78 and 0.79, respectively (Figure 2A-B). These results suggest that the model has good predictive ability

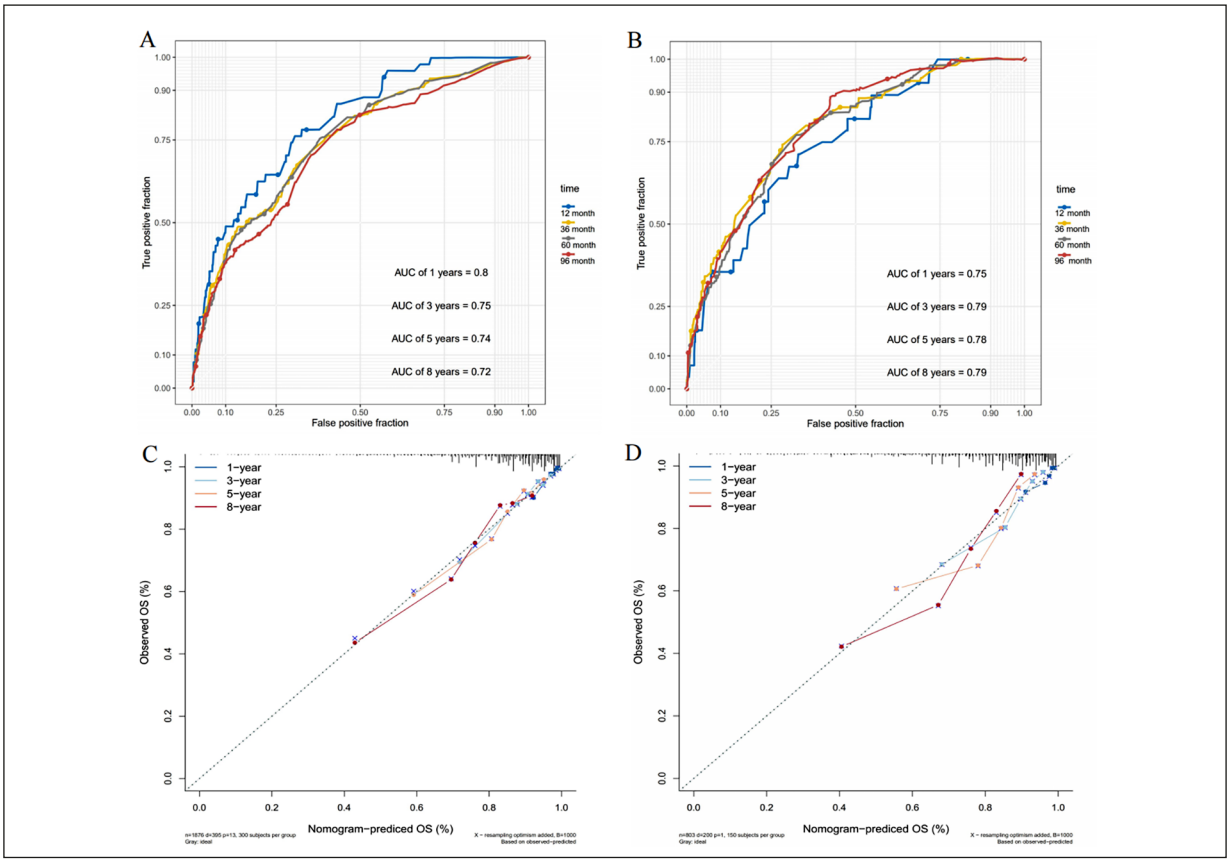

Figure 2. The receiver operating characteristic curve in the training (**A**) and validation cohort (**B**); the calibration curve in the training (**C**) and validation cohort (**D**).

and is superior to traditional TNM staging and SEER stage. The calibration plots (Figure 2C-D) show that the predicted 1-, 3-, 5-, and 8-year survival rates are generally consistent with the actual observations in the two cohorts, with the scatter falling roughly on the 45°, indicating that the nomogram is well calibrated. The above indicators reflect that the model has a high degree of discrimination and consistency. Additionally, the decision curve of our model showed the clinical benefit in Figure 3.

Prognostic Score Value

The independent prognostic indicators of patients were assigned scores according to their weights, and the final risk score model was used to calculate the risk score of each patient. According to the best cutoff of risk score, patients were divided into low-risk group and high-risk group. The log-rank test was used to evaluate the significant difference in prognosis between the two groups. The results showed that in the training group, the hazard ratio (HR) for the high- to low-risk group was 3.27 (95% CI, 2.68-4.00) in 1-year overall survival (OS), 3.67 (95% CI, 2.98-4.54) in 3-year OS, 4.27 (95% CI, 3.40-5.37) in 5-year OS, and 4.58 (95% CI, 3.55-5.90) in 8-year OS (Figure 4). In the validation group, the HR for the high- to low-risk group was 7.22 (95% CI, 4.32-12.07) in 1-year OS, 6.93 (95% CI, 4.60-10.45) in 3-year OS, 5.15 (95% CI, 3.57-7.44) in 5-year OS, and 4.94 (95% CI, 3.54-6.89) in 8-year OS (Figure 5). The differences among the groups were statistically significant ($p < 0.05$).

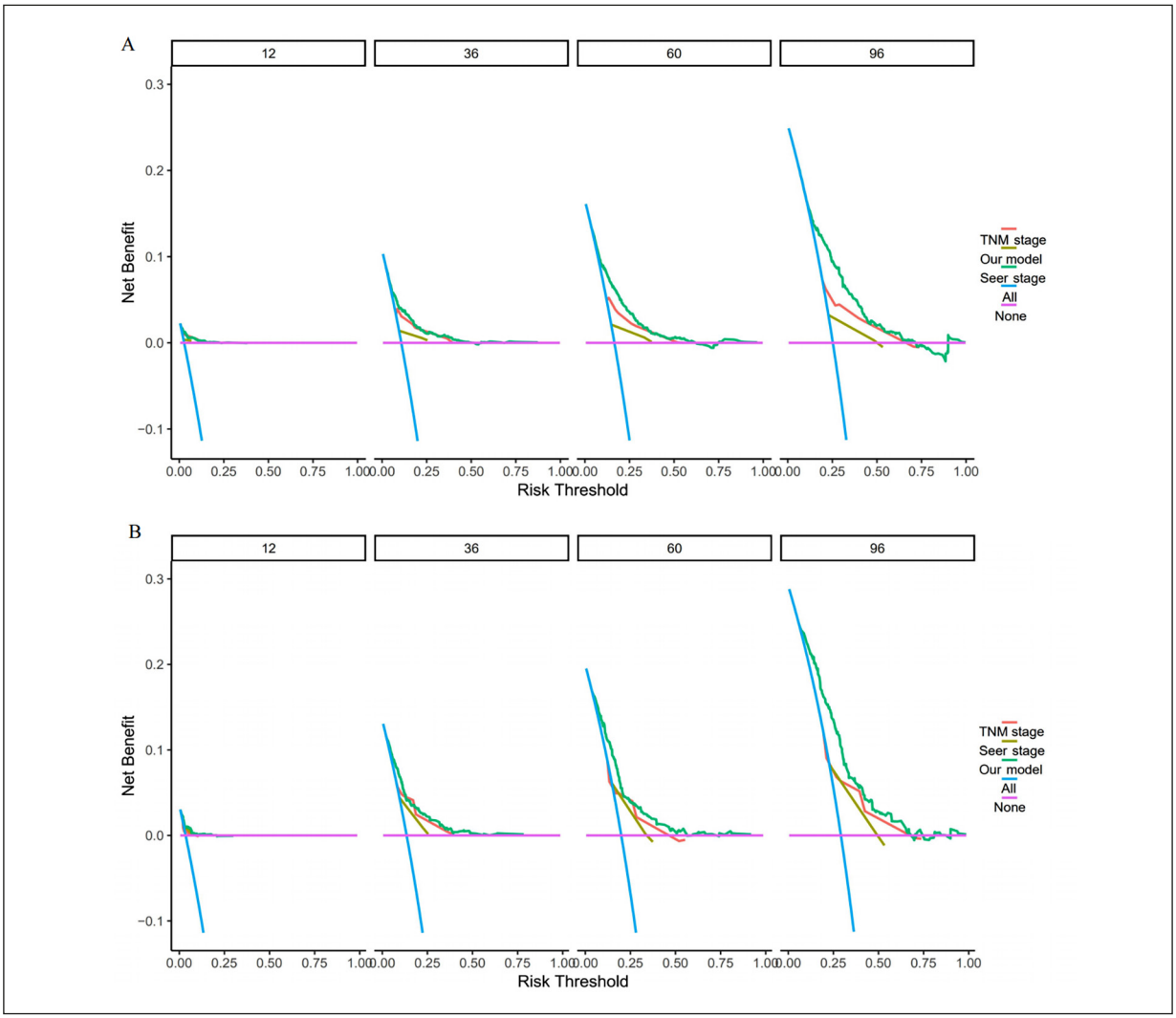

Figure 3. The decision curve in the training (**A**) and validation cohort (**B**).

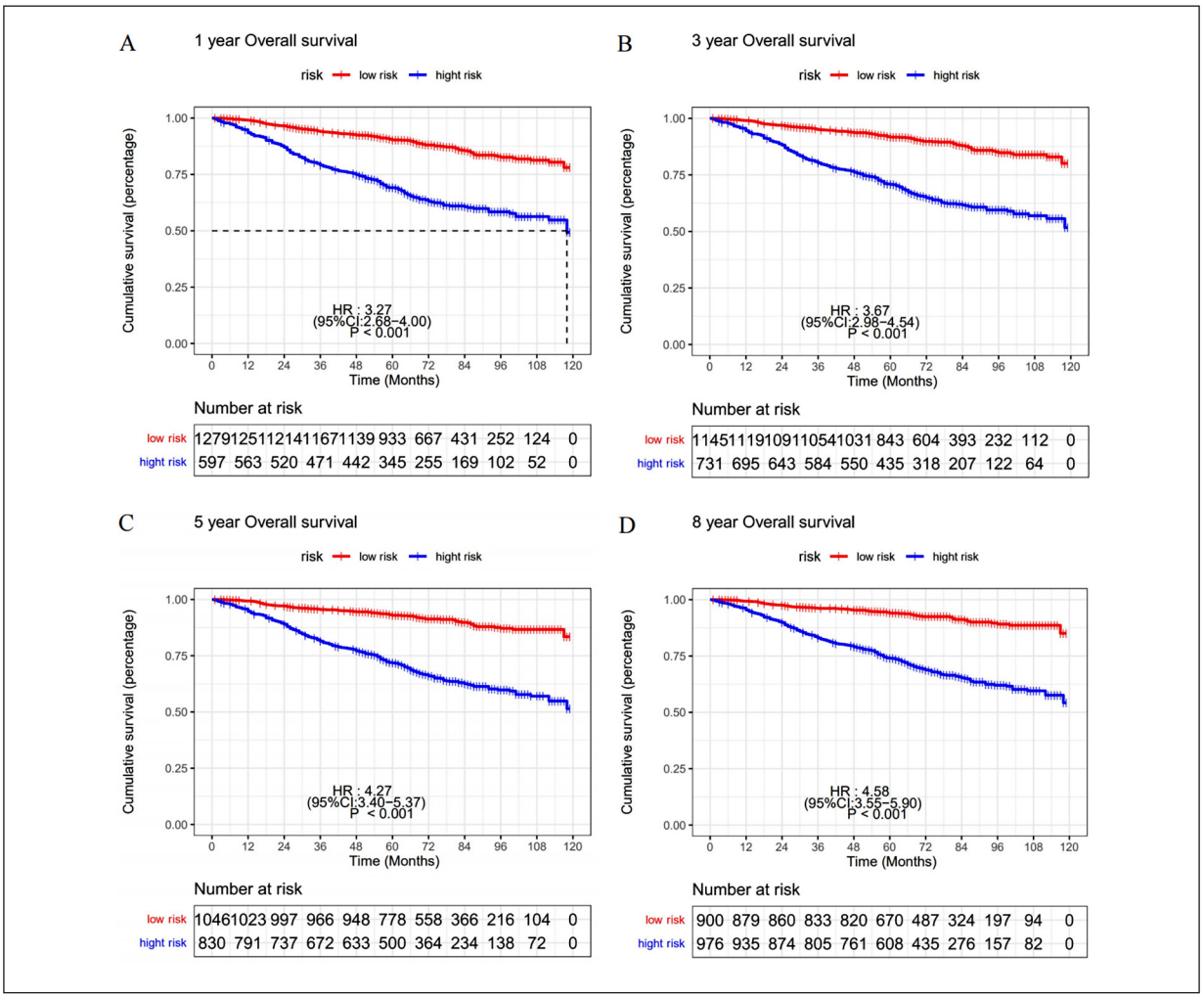

Figure 4. The Kaplan-Meier curve for 1-year (**A**), 3-year (**B**), 5-year (**C**) and 8-year (**D**) overall survival in the training cohort

Discussion

CMM is the most aggressive skin malignant tumor, which is easy to metastasize and can metastasize to almost any tissue in the body[16]. Surgical resection is still the cure method for the treatment of CMM, and radical resection of the primary lesion can enable early patients to achieve long-term disease-free survival[17]. In recent years, with the continuous improvement of the diagnosis rate of malignant melanoma patients, related studies[1] have mushroomed, and the diagnosis and treatment have made great progress, greatly improving the prognosis of malignant melanoma patients. Accurate assessment of the patient's condition is conducive to the personalized treatment and management of patients and is more conducive to further improve their prognosis. At present, tumor stage, presence or absence of ulcer, and thickness are the most reported factors affecting prognosis[18-20]. However, the survival of patients cannot be well evaluated. Prognostic analysis is of great value for the treatment, monitoring and follow-up of tumor patients. For the analysis of prognostic factors of CMM patients, previous studies[21] are mostly limited to small samples and single center, so the bias is large, and no study has provided a prognostic model for CMM. In this study, a total of 2,679 patients with CMM in stage M0 were collected from the SEER database, and the large sample ensured the accuracy and credibility of the model.

Lasso-Cox regression analysis showed that male, multiple tumors, higher T stage, SEER stage, widowed, divorce, separation and family partner often indicated poor prognosis. The

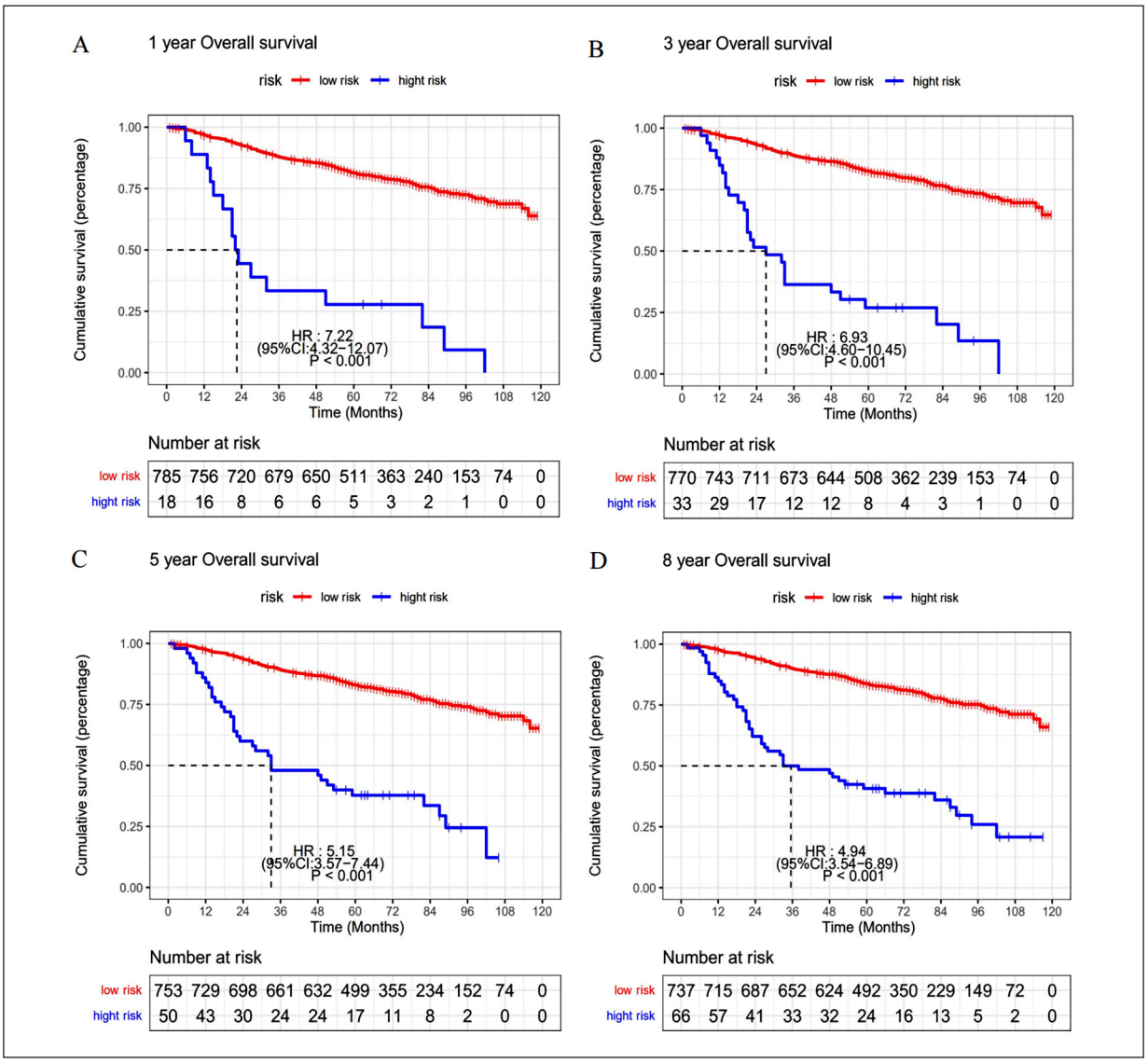

Figure 5. The Kaplan-Meier curve for 1-year (**A**), 3-year (**B**), 5-year (**C**) and 8-year (**D**) overall survival in the validation cohort.

trunk had a better prognosis than the extremities, head, face and neck and other parts of the tumor. However, other conditions had no significant effect on patient survival. Similar to the results of this study, previous studies[22] have suggested that marital status has a certain effect on the overall survival rate of patients. The possible explanation is that marriage can provide more financial or interpersonal support for patients, but divorce and widowhood may cause bad mood, which still needs to be further verified by other studies[22]. In this study, surgery, radiotherapy, chemotherapy, and systemic therapy had no significant effect on cancer-specific survival. Surgery is the main treatment for CMM and has a clear impact on its prognosis. However, the number of patients in this study who did not undergo surgery was too small, resulting in a large bias, so the effect of surgery on prognosis could not be evaluated in this study. Previous studies[22-24] have shown that radiotherapy and chemotherapy improve overall survival, with little effect on cancer-specific survival, which is consistent with our results. Like our findings, male gender has also been identified as a poor prognostic factor for CMM in previous studies[22]. One possible explanation is that men are more likely to smoke or drink alcohol, often leading to poor prognosis. Differ-

ent from the results of our study, older age was also considered to be a poor prognostic factor for CMM[25]. However, the reason for this may be that older patients are more likely to have age-related complications, and the cohort we studied did not have conditions with underlying diseases. In the present study, radiotherapy had no significant effect on tumor-specific survival.

Since TNM stage mainly targets tumor characteristics, it is not difficult to understand that TNM stage has a certain predictive effect on cancer-specific survival. This study confirmed that this T stage has the largest proportion in the nomogram. However, N stage was not included in our study, which may be due to overlap in the evaluation of SEER stage. Our study found independent prognostic factors for SEER stage. Although the TNM staging system has certain predictive ability, its evaluation indicators are too single. The same TNM staging can obtain the same prognosis prediction, but even under the same TNM staging, there is significant heterogeneity in the survival rate of patients. Therefore, in this study, a prediction model including comprehensive indicators was constructed to predict the tumor survival rate of patients with Merkel cell carcinoma, and a nomogram was used to visualize the proportion of multiple prognostic risk factors in the prognosis. In this study, C-index, NRI, IDI, AUC, and calibration curve were used to evaluate the accuracy of the model. In the training group and the validation group, after the data were evaluated by the new model, the evaluation indexes were higher than those of the 7th TNM staging system and SEER stage, and these results proved the superiority of the new model.

The prediction model proposed in this study is the first clinical prediction model of CMM based on a large sample. One of the strengths of this study is the relatively large cohort size, which makes the results more reliable than single-center studies. It is worth mentioning that the prediction performance of this model for tumor-specific survival was better than that of the 7th TNM staging system and the SEER stage. The nomogram can provide individualized prognosis prediction for each patient, which is helpful for clinicians to evaluate the prognosis of patients and formulate personalized treatment plans.

Limitations

This study still has limitations. First, retrospective data may have inherent defects such as entry errors and selection bias. Second, the cases recorded in the SEER database were from the United States, and there are few Asian clinical data records, which may limit the application of the nomogram in China. In addition, due to partial missing or incomplete data in the SEER database, variables that may affect prognosis proposed by other studies, such as sentinel lymph node biopsy results, immunotherapy, sequencing data, etc., were not included in this study.

Conclusions

In summary, sex, SEER stage, T stage, total number of tumors and marital status are independent prognostic factors for CMM patients, and the nomogram model presented a better performance than TNM stage and SEER stage in predicting the prognosis of CMM patients. This study was internally validated, but external validation is needed to further evaluate the accuracy of the model.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Ethics Approval

The data was from public dataset; therefore, the ethics approval was not applicable.

Informed Consent

The data were from public dataset; therefore, the informed consent of patients was not applicable.

Funding

No funding was received for the present study.

References

1) Knackstedt T, Knackstedt RW, Couto R, Gastman B. Malignant Melanoma: Diagnostic and Management Update. Plast Reconstr Surg 2018; 142: 202-216.
2) Ahmed B, Qadir MI, Ghafoor S. Malignant Melanoma: Skin Cancer-Diagnosis, Prevention, and Treatment. Crit Rev Eukaryot Gene Expr 2020; 30: 291-297.
3) Elder DE, Bastian BC, Cree IA, Massi D, Scolyer RA. The 2018 World Health Organization Classification of Cutaneous, Mucosal, and Uveal Mel-

anoma: Detailed Analysis of 9 Distinct Subtypes Defined by Their Evolutionary Pathway. Arch Pathol Lab Med 2020; 144: 500-522.

4) Leonardi GC, Falzone L, Salemi R, Zanghì A, Spandidos DA, Mccubrey JA, Candido S, Libra M. Cutaneous melanoma: From pathogenesis to therapy (Review). Int J Oncol 2018; 52: 1071-1080.
5) Johansson M, Brodersen J, Gøtzsche PC, Jørgensen KJ. Screening for reducing morbidity and mortality in malignant melanoma. Cochrane Database Syst Rev 2019; 6: CD012352.
6) Lopes FCPS, Sleiman MG, Sebastian K, Bogucka R, Jacobs EA, Adamson AS. UV Exposure and the Risk of Cutaneous Melanoma in Skin of Color: A Systematic Review. JAMA Dermatol 2021; 157: 213-219.
7) Petersen B, Philipsen PA, Wulf HC. Skin temperature during sunbathing--relevance for skin cancer. Photochem Photobiol Sci 2014; 13: 1123-1125.
8) Carr S, Smith C, Wernberg J. Epidemiology and Risk Factors of Melanoma. Surg Clin North Am 2020; 100: 1-12.
9) Cabrera R, Recule F. Unusual Clinical Presentations of Malignant Melanoma: A Review of Clinical and Histologic Features with Special Emphasis on Dermatoscopic Findings. Am J Clin Dermatol 2018; 19: 15-23.
10) Ogata D, Namikawa K, Takahashi A, Yamazaki N. A review of the AJCC melanoma staging system in the TNM classification (eighth edition). Jpn J Clin Oncol 2021; 51: 671-674.
11) Yu Z, Hou Y, Zhou W, Zhao Z, Liu Z, Fu A. The effect of mitochondrial transplantation therapy from different gender on inhibiting cell proliferation of malignant melanoma. Int J Biol Sci 2021; 17: 2021-2033.
12) Abdelwahab Yousef AJ. Male Breast Cancer: Epidemiology and Risk Factors. Semin Oncol 2017; 44: 267-272.
13) Lim S, Lee KB, Chon SJ, Park CY. Is tumor size the limiting factor in a laparoscopic management for large ovarian cysts? Arch Gynecol Obstet 2012; 286: 1227-1232.
14) Biondo S, Gálvez A, Ramírez E, Frago R, Kreisler E. Emergency surgery for obstructing and perforated colon cancer: patterns of recurrence and prognostic factors. Tech Coloproctol 2019; 23: 1141-1161.
15) Alattar AA, Brandel MG, Hirshman BR, Dong X, Carroll KT, Ali MA, Carter BS, Chen CC. Oligodendroglioma resection: a Surveillance, Epidemiology, and End Results (SEER) analysis. J Neurosurg 2018; 128: 1076-1083.
16) Thrane K, Eriksson H, Maaskola J, Hansson J, Lundeberg J. Spatially Resolved Transcriptomics Enables Dissection of Genetic Heterogeneity in Stage III Cutaneous Malignant Melanoma. Cancer Res 2018; 78: 5970-5979.
17) Leilabadi SN, Chen A, Tsai S, Soundararajan V, Silberman H, Wong AK. Update and Review on the Surgical Management of Primary Cutaneous Melanoma. Healthcare (Basel) 2014; 2: 234-249.
18) Strömberg U, Peterson S, Holmberg E, Holmén A, Persson B, Sandberg C, Nilbert M. Cutaneous malignant melanoma show geographic and socioeconomic disparities in stage at diagnosis and excess mortality. Acta Oncol 2016; 55: 993-1000.
19) Alexandru Gata V, Milan Kubelac P, Buiga R, Vlad IC, Valean D, Muntean MV, Morariu DS, Bonci EA, Irimie A, Dina C, Achimas Cadariu PA. The value of tumor infiltrating lymphocytes as prognostic factor for lymph node status and survival amongst patients with cutaneous malignant melanoma. J BUON 2020; 25: 2700-2707.
20) Harvima IT, Harvima RJ. Survival from cutaneous malignant melanoma is improving, but is it because of a trend in decreasing melanoma thickness or the advent of new 'revolutionary' therapeutics? Br J Dermatol 2022; 187: 6-7.
21) Simberg-Danell C, Lyth J, Månsson-Brahme E, Frohm-Nilsson M, Carstensen J, Hansson J, Eriksson H. Prognostic factors and disease-specific survival among immigrants diagnosed with cutaneous malignant melanoma in Sweden. Int J Cancer 2016; 139: 543-553.
22) Ai L, Li N, Tan HL, Wei B, Zhao YX, Chen P, Hu HY, Liu M, Ou-Yang DJ, Qin ZE, Huang P, Chang S. Effects of marital status on survival of medullary thyroid cancer stratified by age. Cancer Med 2021; 10: 8829-8837.
23) Mendenhall WM, Amdur RJ, Morris CG, Kirwan J, Shaw C, Dziegielewski PT. Adjuvant postoperative radiotherapy for cutaneous melanoma. Acta Oncol 2017; 56: 495-496.
24) Luke JJ, Schwartz GK. Chemotherapy in the management of advanced cutaneous malignant melanoma. Clin Dermatol 2013; 31: 290-297.
25) Tas F, Erturk K. Patient age and cutaneous malignant melanoma: Elderly patients are likely to have more aggressive histological features and poorer survival. Mol Clin Oncol 2017; 7: 1083-1088.