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ORIGINAL RESEARCH

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Establishment and validation of a nomogram for estimating the overall survival of vulvar squamous cell carcinoma patients aged 50 years or older

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Abstract

This study aimed to develop a nomogram for estimating the overall survival (OS) of vulvar squamous cell carcinoma patients aged ≥50 years based on their clinicopathological characteristics. The Surveillance, Epidemiology and End Results (SEER) database was searched for cases diagnosed with vulvar squamous cell carcinoma from 2000 to 2019. They were randomly grouped into a training and a test cohort in a 7:3 ratio. Cox regression analyses were performed to identify risk factors associated with the overall survival rate of the patients. Then, the nomogram was built based on independent factors selected by the minimum Akaike Information Criterion (AIC) value in multivariate Cox regression analyses. The performance of the nomogram was assessed by its concordance index (C-index) and the area under curve (AUC). Its predictive power was determined by calibration plot and clinical applicability by decision curve analysis (DCA). A total of 3048 patients were identified and randomized into the training (n = 2146) and validation (n = 902) cohort. The validation indicated that the nomogram had good recognition ability for clinical trials, patient counseling, and rationalizing therapeutic modalities. The C-index for OS rates was 0.729 (95% Confidence Interval (CI): 0.715–0.743) in the training cohort and 0.717 (95% CI: 0.693–0.741) in the validation cohort. The AUCs of the 1-, 3- and 5-year OS were 0.789, 0.781 and 0.775 in the training cohort and 0.815, 0.772 and 0.748 in the validation cohort. Calibration plots showed that the nomogram had good predictive power, and DCA demonstrated that the proposed nomogram could provide a net clinical benefit. Our nomogram demonstrated promising accuracy in comprehensively predicting the OS of elderly vulvar squamous cell carcinoma patients. It could be used as a reference to guide individualized treatments and plan the follow-up of elderly patients with vulvar squamous cell carcinoma.

Keywords

Overall survival; Prognosis; Nomogram; Vulvar squamous cell carcinoma; SEER

1. Introduction

As the fourth most common gynecologic tumor [1], the primary malignant tumor of the vulva accounts for 4% of all cancers of the female genital tract [2]. It is more prevalent in elderly women and has a median age at diagnosis of about 68 years [3, 4]. From 2001 to 2017, the incidence rate of vulvar cancer related to human papilloma virus (HPV) in the United States increased by 1.2% every year, especially among women aged 50–69, while the overall incidence rate of non-HPV-related cancer remained stable [5]. Comparatively, a South Korean population-based study from 2014 to 2018 showed no significant change in the incidence of vulvar cancer during a similar time period [6]. According to the estimation of the American Cancer Association, there will be an estimated 6330 new vulvar cancer cases and 1560 related death in 2022 [1]. Most vulvar cancer cases (>90%) are squamous cell carcinoma (SCC), while the remaining are pathologically classified as melanoma, adenocarcinoma, basal cell carcinoma, sarcoma and undifferentiated tumors [7]. Based on its morphological differences, vulvar squamous cell carcinoma (VSCC) can be divided into keratinizing, basaloid, warty and verrucous types. Although vulvar cancer could be asymptomatic, its frequent clinical manifestations include vulvar pruritus, bloody vaginal secretions, palpable vulvar masses or pain [3]. Clinically, skin lesions are characterized by skin thickening or discoloration, flattening, swelling, ulceration or plaque-like lesions [3]. About 59% of vulvar carcinoma patients present with a localized lesion, while 30% present with regional lymph node metastasis and 6% with distant site metastasis [3, 8], and have been reported to associate with a 5-year survival rate of 86%, 53% and 19%, respectively [8].

The increase in the aging population has led to an increase in the number of elderly patients. In addition, considering that elderly patients might have degenerative diseases or comorbidities, they often have poor surgical tolerance and may experience serious adverse events with radiotherapy or chemotherapy. Thus, complications in elderly patients might lead to poor prognosis and high mortality unless properly treated. The staging system of the International Federation of Obstetricians and Gynaecologists (FIGO) is commonly used to stage vulvar cancer and estimate the patient's prognosis [9]. However, considering that vulvar cancer is multifactorial, the FIGO classification might have limited prognostic accuracy because it only considers the impact of tumor characteristics such as tumor size, invasion depth, lymph node status and metastasis and does not consider individual differences affecting the patient's prognosis, such as age, tumor grade and effects of radiotherapy and chemotherapy. Therefore, it is necessary to develop a new method that could include more patient-, tumor- and treatment-related characteristics to more accurately predict patients' survival and could be important to guide their management.

Nomogram is a widely used graphical scoring model that combines various independent risk factors to predict the overall survival of cancer patients [10, 11]. Presently, there are limited studies on nomograms for vulvar cancer [12–16] and none for elderly vulvar cancer patients. Considering that these patients are at high risk of developing complications and mortality, it is very important to identify prognostic factors that could affect their prognosis, accurately estimate their overall survival and develop individualized treatments that could improve their outcomes.

Thus, the present study was designed to identify and assess the clinicopathological factors of vulvar squamous cell carcinoma patients aged over 50 years and establish a nomogram that could incorporate these variables to more accurately predict their overall survival. Additionally, the receiver operating characteristic (ROC) curve, calibration curve and DCA curve were implemented to evaluate the accuracy, predictive value and clinical applicability of our proposed prediction model.

2. Methods

2.1 Data retrieval

The SEER database (http://www.seer.cancer.gov), which covers approximately 34.6% of the US population [17], was used to obtain the demographics, primary tumor location, tumor stage, surgical treatment, survival time and other data of vulvar squamous cell carcinoma patients. We obtained access to the Incidence—SEER Research Plus Data database, 17 Registries, Nov 2021 Sub (2000–2019), based on the November 2021 submission using the SEER*Stat software (version 8.4.0; Surveillance Research Program, NCI, Bethesda, MD, USA).

2.2 Patients

The study inclusion criteria were: (1) cases that matched the International Classification of tumor diseases 3 (ICD-O-3) codes 8070, 8071, 8072, 8083 and 8090, and (2) had active follow-up data to ensure reliable patient status. Cases with missing follow-up data, American Joint Committee on Cancer (AJCC) stage classification, grade, tumor size, tumor-node-metastasis (TNM) stage, lymph node resection status and treatment (*i.e.*, surgery, radiotherapy and chemotherapy) were excluded from this study. The eligible cases were then grouped randomly into a training and a test cohort in a 7:3 ratio (Fig. 1).

2.3 Measurable variables

This study used age, grade, tumor size, the AJCC, TNM and summary stage, primary site and local lymph node surgery, local lymph node postoperative pathology, and whether radiotherapy and chemotherapy were studied. The training cohort was used to construct the nomogram, while the validation cohort was used for validation analysis. The patients were divided into the age groups 50–59, 60–69, 70–79 and above 80 years old. Tumor grade was divided into well-differentiated (I), moderately differentiated (II), poorly differentiated (III) and undifferentiated (IV), tumor size into <4 cm and ≥ 4 cm, the AJCC and TNM stage as generally acknowledged, and the summary stage was divided into local, regional and distant. Surgery (including primary site surgery and regional lymph node surgery), chemotherapy and radiotherapy were divided into receiving and not receiving therapy. Local lymph node status was divided into positive or negative. The study endpoint was OS, which was labeled as "survival months".

2.4 Statistical analysis

Descriptive statistical analysis was used for age and clinical factors. The chi-square test was used for correlation analysis between the SEER cohorts (Table 1). Significant variables in univariate analysis ($p < 0.05$) were included for multivariate Cox regression analysis, and forced, forward, backward and stepwise regression methods were used to analyze them. Using the Akaike information criterion (AIC) minimum selection optimal model, we established a nomogram that could predict the 1-, 3- and 5-year OS of vulvar cancer patients aged ≥ 50 years. The discrimination ability of the nomogram is evaluated using the concordance index (C-index) or ROC in both the training and validation cohorts. The consistency between the predicted and actual OS probability was quantitatively estimated.

The model was considered reliable for C-index values 0.51–0.7, to have clinical significance for C-index values 0.7–0.89, and to possess high reliability and prediction ability for C-index values ≥ 0.9. Calibration was determined by comparing the association between the frequency of observations and prediction probability through 500 repeated samples. The 45-degree diagonal line on the calibration graph indicates perfect absolute risk estimation. At the same time, DCA was performed to assess the clinical significance of the proposed nomogram by quantifying the net outcome under different threshold probabilities.

The Chi-square test was conducted using the IBM SPSS v26.0 statistical software (SPSS, Inc, Chicago, IL, USA). Univariate and multivariate analysis, nomogram construction, ROC analysis, model calibration and DCA were carried out using the R v4.1.2 software (R Development Core Team,

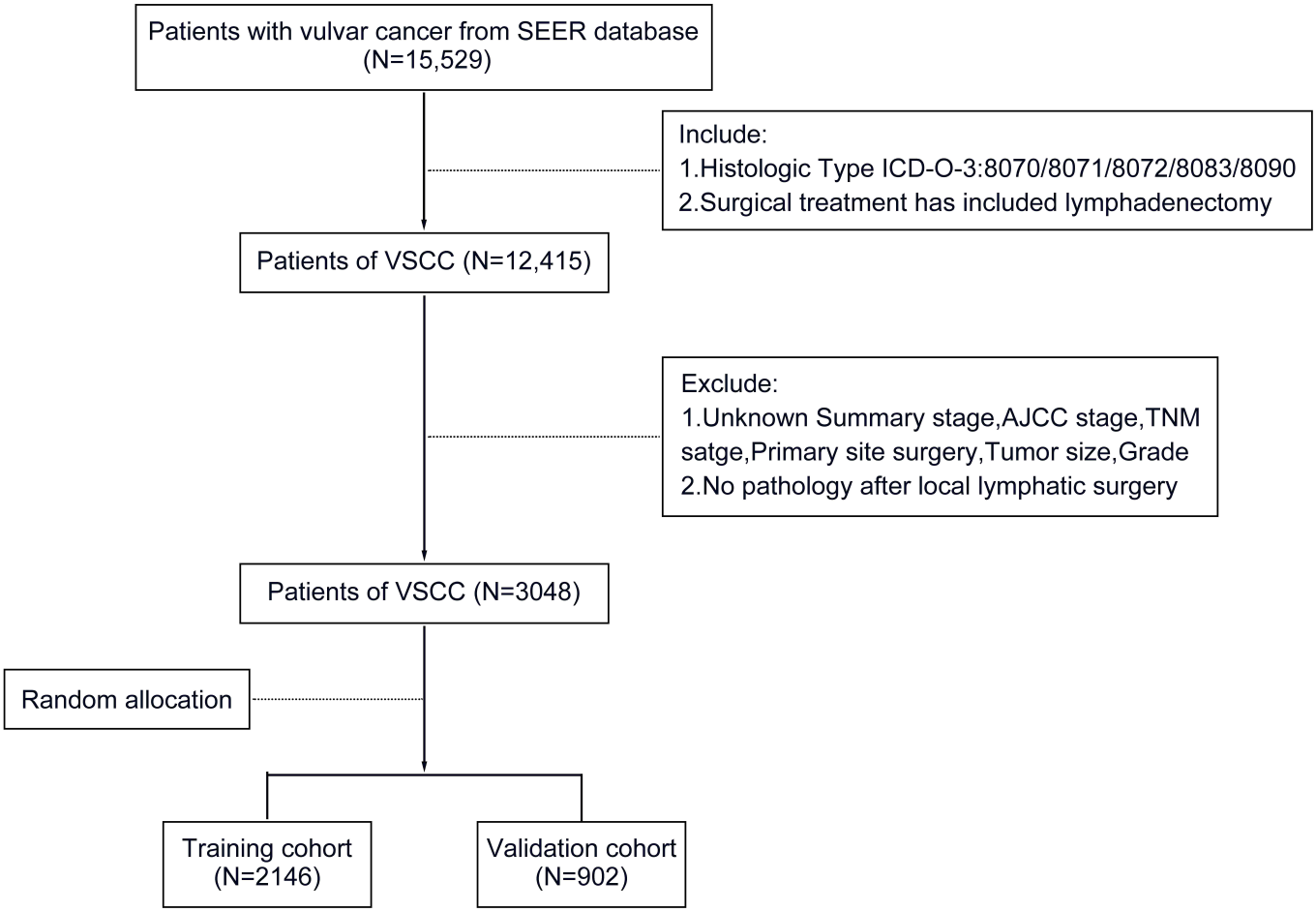

FIGURE 1. Flowchart for patient selection. SEER: Surveillance, Epidemiology and End Results; ICD-O-3: International Classification of tumor diseases 3; VSCC: vulvar squamous cell carcinoma; AJCC: American Joint Committee on Cancer; TNM: tumor-node-metastasis.

The University of Auckland) (http://www.r-project.org). Two-sided *p*-values (<0.05) were considered statistically significant.

3. Result

3.1 Baseline characteristics of the study cohort

In total, 3048 patients were eligible for this study, and the proportion of patients in each age group was approximately 25% (Table 1). In terms of clinical factors, the tumor size of 69.3% of patients was less than 4 cm, and only 0.9% of the patients were diagnosed with an undifferentiated vulvar tumor. Among all included patients, the proportion of distant metastasis was 2.7%, which was also consistent with the AJCC stage and TNM stage in the table. Additionally, 97.4% and 98.2% of the patients underwent surgery on the primary site and localized lymph nodes, respectively, and the positive rate of lymph nodes was 33.8%. Further, 30.4% and 13.6% of the patients from the entire cohort underwent radiotherapy and chemotherapy.

3.2 Independent factors for the nomogram

Table 2 illustrates the significant factors in univariate Cox regression analysis and independent factors in multivariate Cox regression analysis associated with the OS of patients with vulvar cancer. According to the AIC minimum principle, the backward method was used to assess the seven factors to be included in the nomogram, which were age, summary stage, AJCC stage, T stage, chemistry recode, regional nodes status and tumor size.

3.3 Nomogram construction and validation

Using the above seven factors, we established a nomogram that could predict the 1-, 3- and 5-year OS of vulvar squamous cell carcinoma patients aged $\geq$50 years. As shown in Fig. 2, age was the most critical factor affecting the survival rate of the patients, followed by the AJCC stage, local lymph node positivity, summary stage, tumor size, chemotherapy and T stage. The C-index of the training and validation cohort was 0.729 (95% CI, 0.715–0.743) and 0.717 (95% CI, 0.693–0.741), respectively. The high internal and external verification C-index values indicated the good discrimination performance of the nomogram. The AUCs of the 1-, 3- and 5-year OS rate was 0.789, 0.781 and 0.775 in the training cohort and 0.815, 0.772 and 0.748 in the validation cohort, respectively, which

TABLE 1. Baseline age and clinical characteristics of vulvar squamous cell cancer patients from SEER database.

Variables	Total (N = 3048) (%)	Training cohort (N = 2146) (%)	Validation cohort (N = 902) (%)	*p*-value
Age at diagnosis (year)				
50~59	703 (23.1)	495 (23.1)	208 (23.1)	0.107
60~69	775 (25.4)	526 (24.5)	249 (27.6)	
70~79	842 (27.6)	589 (27.4)	253 (28.0)	
≥80	728 (23.9)	536 (25.0)	192 (21.3)	
Summary stage				
Distant	81(2.7)	56(2.6)	25(2.8)	0.908
Localized	1548 (50.8)	1086 (50.6)	462 (51.2)	
Reginal	1419 (46.6)	1004 (46.8)	415 (46.0)	
AJCC stage				
I	902 (29.6)	635 (29.6)	267 (29.6)	0.754
II	962 (31.6)	675 (31.5)	287 (31.8)	
III	880 (28.9)	614 (28.6)	266 (29.5)	
IV	304 (10.0)	222 (10.3)	82 (9.1)	
T stage				
T1	1094 (35.9)	762 (35.5)	332 (36.8)	0.852
T2	1634 (53.6)	1160 (54.1)	474 (52.5)	
T3	287 (9.4)	202 (9.4)	85 (9.4)	
T4	33 (1.1)	22 (1.0)	11 (1.2)	
N stage				
N0	2002 (65.7)	1402 (65.3)	600 (66.5)	0.516
N1	800 (26.2)	563 (26.2)	237 (26.3)	
N2	246 (8.1)	181 (8.4)	65 (7.2)	
M stage				
M0	2986 (98.0)	2102 (97.9)	884 (98.0)	0.922
M1	62 (2.0)	44 (2.1)	18 (2.0)	
Primary site surgery				
No	80 (2.6)	60 (2.8)	20 (2.2)	0.362
Yes	2968 (97.4)	2086 (97.2)	882 (97.8)	
Local lymph node surgery				
No	56 (1.8)	36 (1.7)	20 (2.2)	0.311
Yes	2992 (98.2)	2110 (98.3)	882 (97.8)	
Radiation recode				
No/Unknown	2121 (69.6)	1493 (69.6)	628 (69.6)	0.977
Yes	927 (30.4)	653 (30.4)	274 (30.4)	
Chemotherapy recode				
No/Unknown	2632 (86.4)	1853 (86.3)	779 (86.4)	0.990
Yes	416 (13.6)	293 (13.7)	123 (13.6)	
Regional nodes positive				
Negative	2017 (66.2)	1411 (65.8)	606 (67.2)	0.445
Positive	1031 (33.8)	735 (34.2)	296 (32.8)	
Tumor size (cm)				
<4	2112 (69.3)	1478 (68.9)	634 (70.3)	0.439
≥4	936 (30.7)	668 (31.1)	268 (29.7)	
Grade				
I	780 (25.6)	538 (25.1)	242 (26.8)	0.329
II	1591 (52.2)	1126 (52.5)	465 (51.6)	
III	651 (21.4)	467 (21.8)	184 (20.4)	
IV	26 (0.9)	15 (0.7)	11 (1.2)	

AJCC: American Joint Committee on Cancer.

TABLE 2. Univariate and multivariate analysis of the training cohort.

Variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
Age at diagnosis (year)				
50~59	Reference		Reference	
60~69	1.71 (1.406–2.079)	<0.001***	1.65 (1.352–2.004)	<0.001***
70~79	2.57 (2.141–3.088)	<0.001***	2.48 (2.058–2.981)	<0.001***
≥80	4.63 (3.865–5.546)	<0.001***	4.63 (3.838–5.573)	<0.001***
Summary stage				
Distant	Reference		Reference	
Localized	0.21 (0.156–0.279)	<0.001***	0.29 (0.191–0.444)	<0.001***
Regional	0.39 (0.296–0.526)	<0.001***	0.35 (0.237–0.502)	<0.001***
AJCC stage				
I	Reference		Reference	
II	1.89 (1.619–2.214)	<0.001***	1.17 (0.879–1.564)	0.279
III	2.67 (2.282–3.114)	<0.001***	0.71 (0.456–1.093)	0.118
IV	4.87 (4.028–5.895)	<0.001***	1.10 (0.673–1.788)	0.711
T stage				
T1	Reference		Reference	
T2	2.09 (1.837–2.372)	<0.001***	1.25 (0.971–1.606)	0.083
T3	2.21 (1.811–2.694)	<0.001***	1.40 (1.024–1.904)	0.035*
T4	3.21 (1.996–5.158)	<0.001***	0.50 (0.270–0.923)	0.027*
N stage				
N0	Reference			
N1	2.15 (1.899–2.426)	<0.001***		
N2	3.46 (2.894–4.126)	<0.001***		
M stage				
M0	Reference			
M1	4.20 (3.061–5.745)	<0.001***		
Primary site surgery				
No	Reference			
Yes	0.64 (0.470–0.883)	0.006**		
Local lymph node surgery				
No	Reference			
Yes	0.74 (0.491–1.103)	0.137		
Radiation status				
No/Unknown	Reference			
Yes	1.56 (1.392–1.756)	<0.001***		
Chemotherapy status				
No/Unknown	Reference		Reference	
Yes	1.25 (1.065–1.458)	0.006**	0.84 (0.703–1.003)	0.054
Regional nodes status				
Negative	Reference		Reference	
Positive	2.41 (2.151–2.689)	<0.001***	2.71 (1.940–3.786)	<0.001***
Tumor size (cm)				
<4	Reference		Reference	
≥4	2.03 (1.810–2.271)	<0.001***	1.34 (1.172–1.528)	<0.001***
Grade				
I	Reference			
II	1.31 (1.136–1.501)	<0.001***		
III	1.51 (1.280–1.773)	<0.001***		
IV	1.00	0.996		

****p < 0.001, **p < 0.01, *p < 0.05.*

AJCC: American Joint Committee on Cancer. HR: Hazard Ratio. CI: Confidence Interval.

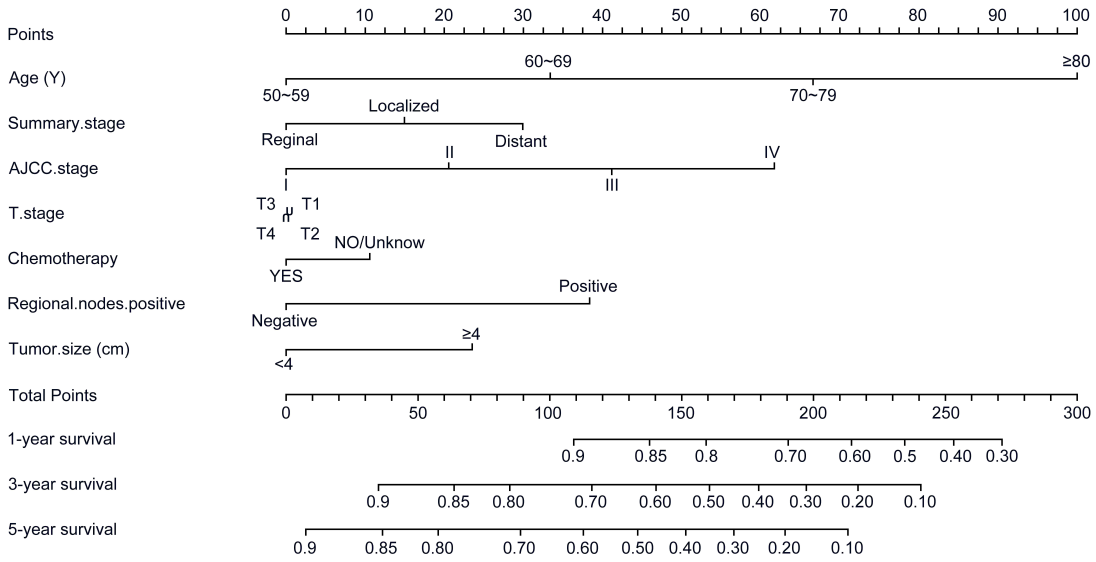

FIGURE 2. Nomogram for predicting the 1-, 3- and 5-year overall survival rates of patients with vulvar squamous cell carcinoma patients aged 50 years or older. AJCC: American Joint Committee on Cancer.

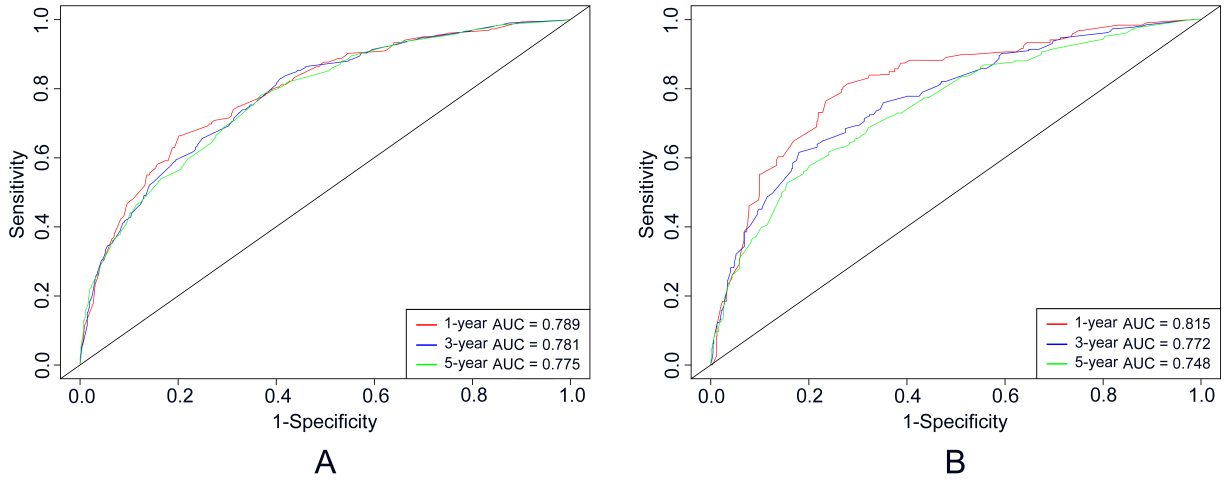

FIGURE 3. ROC curve analysis for predicting the 1-, 3- and 5-year overall survival rates of patients of vulvar squamous cell carcinoma patients aged 50 years or older. (A) ROC curve for the training cohort. (B) ROC curve for the validation cohort. AUC: area under curve. ROC: receiver operating characteristic.

demonstrated the good discrimination ability of our proposed nomogram (Fig. 3). Additionally, good consistency was observed between the observed and predicted OS probability in both the training and validation cohorts (Fig. 4). DCA results showed that it was preferable to apply this model than to let all patients or no patients receive treatment within the threshold probability range (Fig. 5).

4. Discussion

In this present study, age, summary stage, AJCC stage, T stage, chemotherapy, regional nodes status and tumor size were identified as independent factors associated with the OS of vulvar squamous cell carcinoma patients aged ≥50 years old, which were then used to build and validate a nomogram for predicting patient's OS, and could also be used as a reference for making personalized disease monitoring and treatment decisions.

Our analysis showed that most vulvar squamous cell carcinomas were diagnosed at localized and regional stages, and the differentiation type was grade II (intermediate differentiation), which was consistent with previous literature reports [18, 19]. Previous studies also identified age as an important independent prognostic factor associated with patients' survival and that older patients were at higher risk for poorer OS rate [13, 20, 21], similar to that observed in our analysis. However, a previous study reported that the relationship between age and overall patient survival was uncertain [22]. We also observed that chemotherapy was associated with improved OS, which was concordant with Mao Y *et al.* [14] and Vulcan *et al.* [23]. However, Scampa *et al.* [16] contrastingly observed that chemotherapy was not associated with OS benefits, possibly because it was mostly prescribed in patients with advanced diseases, thereby demonstrating lower survival rates.

In addition, our study showed that a higher T stage was associated with higher OS. Although this variable accounted for a small proportion of the nomogram, it cannot be ignored

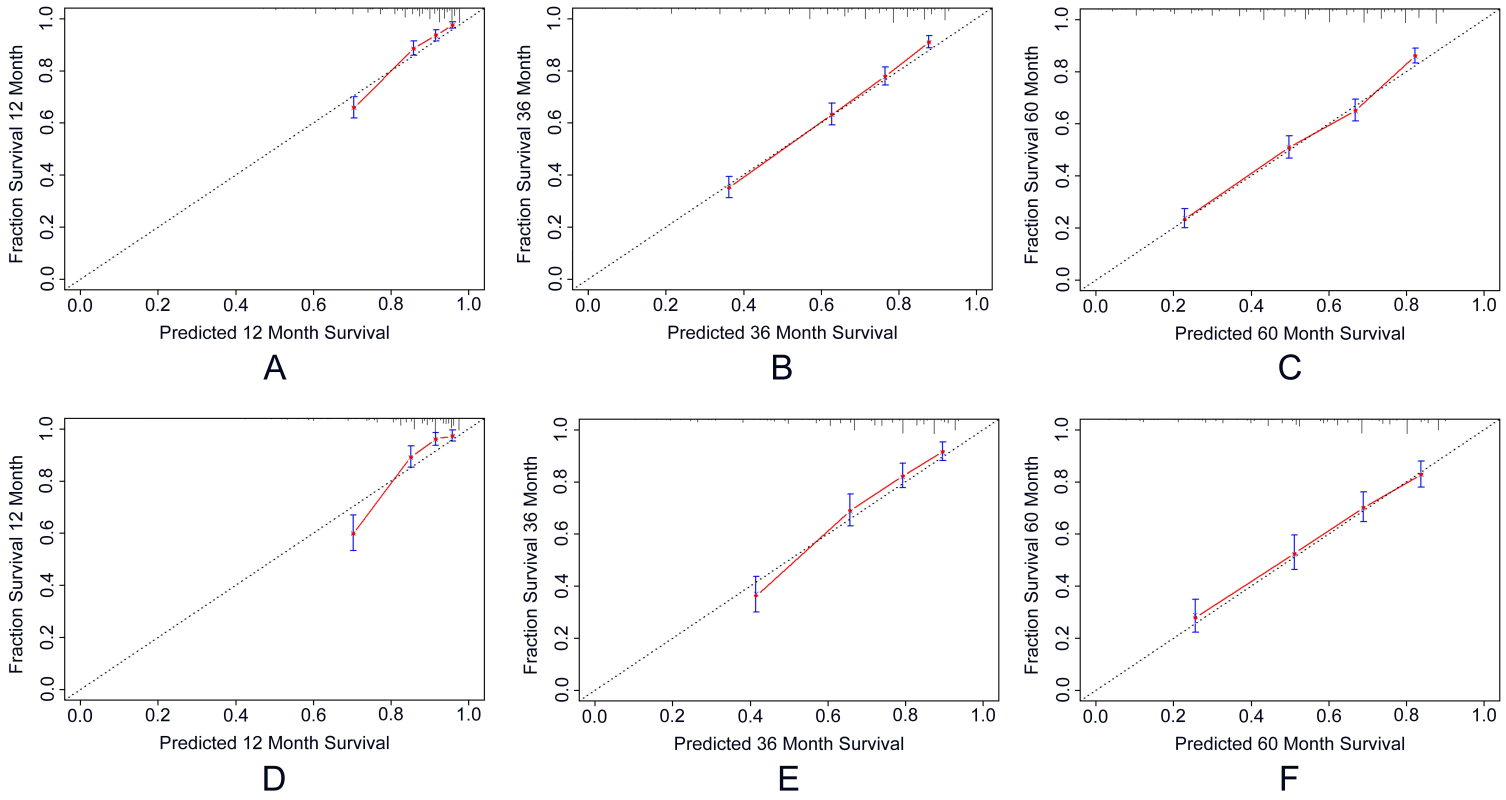

FIGURE 4. Calibration plots of the nomogram for predicting the 1-, 3- and 5-year overall survival rates of patients of vulvar squamous cell carcinoma patients aged 50 years or older. Calibration plots showing the relationship between the predicted probabilities based on the nomogram predicted values and the actual values of the training (A–C) and validation cohorts (D–F).

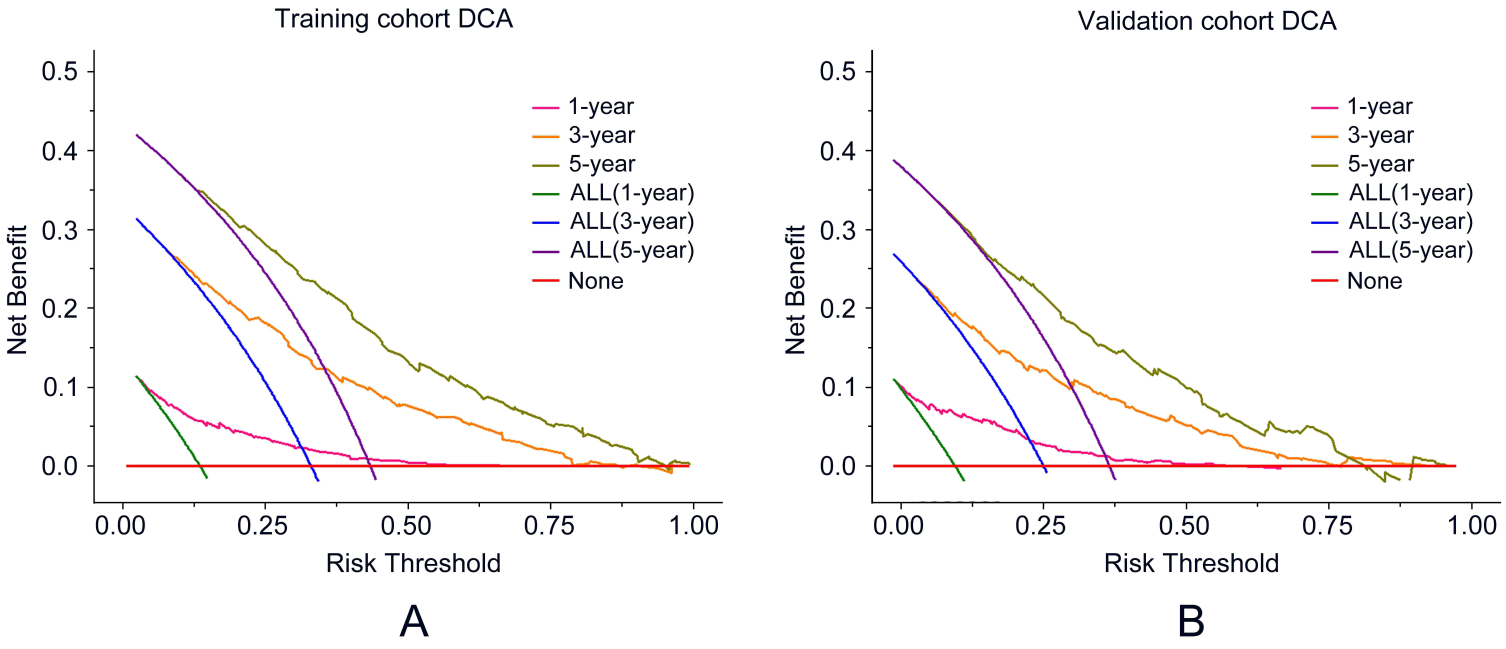

FIGURE 5. DCA of the 1-, 3- and 5-year overall survival rates for the training and validation cohorts. (A) The DCA of the 1-, 3- and 5-year overall survival rates for the training cohort; (B) The DCA of the 1-, 3- and 5-year overall survival rates for the validation cohort. The abscissa represents the threshold probability and the ordinate represents the net benefit rate. The X-axis indicates that all samples are negative and all are not treated, with a net benefit of zero. The green, blue, purple lines indicate that all samples are positive for 1-, 3- and 5-year. The net benefit is represented by a negative slope. The DCA showed that predicting the 1-, 3- and 5-year OS rates using this nomogram would be better than having all patients or none patients treated by this nomogram with a range of the threshold probability. DCA: decision curve analysis.

due to inconsistency with previous studies [14]. We consider that this observation could be related to the inevitable selection bias of the SEER database. Further, similar to previous studies which showed that positive inguinal lymph node and lymph node ratio (LNR) >0.2 were important factors affecting the survival of vulvar cancer patients [24, 25], our results also showed that localized lymph node positivity was an important risk factor independently related with the OS of the patients.

This study had some limitations. First, although race was not an independent factor for consideration during establishing the nomogram, most of the patients were white, and thus, its clinical applicability for other ethnic groups required further investigations. Second, the retrospective nature of this study makes it vulnerable to potentially inevitable inherent bias during patient selection. Third, HPV infection was not included in the nomogram. A retrospective study found that the incidence rate of HPV-related VSCC in New Zealand significantly increased from 1990 to 2016, especially in elderly women aged more than 50 years [26]. However, contradicting results were also reported, which suggested that HPV-unrelated VSCC was more common than HPV-related tumors in elderly women and were associated with worse prognoses [27]. We hypothesized that these differences could be related to the studied population and geography, and future and better-designed research is required to confirm the correlation between vulvar squamous cell carcinoma and HPV and the prognosis of elderly women in China. Fourth, this study lacked external validation to confirm its significance as a clinically applicable prediction tool. Fifth, we did not analyze the tumor-specific death of elderly patients with high accidental risks of death. Lastly, we did not evaluate the clinical applicability of this nomogram compared with the current FIGO staging system.

In conclusion, we constructed and internally validated a nomogram able to evaluate the 1-, 3-, and 5-year OS of VSCC patients aged ≥50 years. It could also be used to stratify patients based on their estimated survival and provide a reference for individualized treatment after surgery.

AVAILABILITY OF DATA AND MATERIALS

The authors declare that all data supporting the findings of this study are available within the paper, and any raw data can be obtained from the corresponding author upon request.

AUTHOR CONTRIBUTIONS

YQQ—designed and conducted this study; YQQ, SFX, SFW and YC—supervised, analyzed and interpreted the data; YQ and YZ—prepared the manuscript for publication and reviewed the draft of the manuscript. All authors have read and approved the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] Virarkar M, Vulasala SS, Daoud T, Javadi S, Lall C, Bhosale P. Vulvar cancer: 2021 revised FIGO staging system and the role of imaging. Cancers. 2022; 14: 2264.

[2] Pedrão PG, Guimarães YY, Godoy LR, Possati-Resende JC, Bovo AC, Andrade CEMC, *et al*. Management of early-stage vulvar cancer. Cancers. 2022; 14: 4184.

[3] Chow L, Tsui BQ, Bahrami S, Masamed R, Memarzadeh S, Raman SS, *et al*. Gynecologic tumor board: a radiologist's guide to vulvar and vaginal malignancies. Abdominal Radiology. 2021; 46: 5669–5686.

[4] Merlo S. Modern treatment of vulvar cancer. Radiology and Oncology. 2020; 54: 371–376.

[5] Mix JM, Gopalani SV, Simko S, Saraiya M. Trends in HPV- and non-HPV-associated vulvar cancer incidence, United States, 2001–2017. Preventive Medicine. 2022; 164: 107302.

[6] Ouh Y, Kang D, Kim H, Lee JK, Hong JH. Prevalence and treatment of vulvar cancer from 2014–2018: a nationwide population-based study in Korea. Journal of Korean medical science. 2022; 37: e25.

[7] Weinberg D, Gomez-Martinez R. Vulvar cancer. Obstetrics and Gynecology Clinics. 2019; 46: 125–135.

[8] Serrado MA, Horta M, Cunha TM. State of the art in vulvar cancer imaging. Radiologia Brasileira. 2019; 52: 316–324. (In Portuguese)

[9] Olawaiye AB, Cuello MA, Rogers LJ. Cancer of the vulva: 2021 update. International Journal of Gynecology & Obstetrics. 2021; 155: 7–18.

[10] Deng CG, Lv Y, Yan H, Sun DC, Qu TT, Pan YT, *et al*. Nomogram to predict survival of patients with advanced and metastatic pancreatic Cancer. BMC Cancer. 2021; 21: 1227.

[11] Xiao R, Liu C, He W, Ma L. Prognostic factors and a nomogram predicting overall survival and cancer-specific survival for patients with collecting duct renal cell carcinoma. BioMed Research International. 2021; 2021: 1–15.

[12] Rouzier R, Preti M, Haddad B, Martin M, Micheletti L, Paniel B. Development and validation of a nomogram for predicting outcome of patients with vulvar cancer. Obstetrics & Gynecology. 2006; 107: 672–677.

[13] Lei L, Tan L, Zhao X, Zeng F, Xu D. A prognostic nomogram based on lymph node ratio for postoperative vulvar squamous cell carcinoma from the surveillance, epidemiology, and end results database: a retrospective cohort study. Annals of Translational Medicine. 2020; 8: 1382.

[14] Mao Y, He M, Tang Z, Chen M, Wu L, Liang T, *et al*. Prognostic nomograms to predict overall survival and cause specific death in vulvar squamous cell carcinoma. International Journal of Gynecologic Cancer. 2022; 32: 706–715.

[15] Liu J, Wang M. Development and validation of nomograms predicting cancer-specific survival of vulvar cancer patients: based on the surveillance, epidemiology, and end results program. International Journal of Gynecology & Obstetrics. 2022; 156: 529–538.

[16] Scampa M, Kalbermatten DF, Oranges CM. Squamous cell carcinoma of the vulva: a survival and epidemiologic study with focus on surgery and radiotherapy. Journal of Clinical Medicine. 2022; 11: 1025.

[17] Pan X, Yang W, Chen Y, Tong L, Li C, Li H. Nomogram for predicting the overall survival of patients with inflammatory breast cancer: a SEER-based study. The Breast. 2019; 47: 56–61.

[18] Hellman K, Holmberg E, Bjurberg M, Borgfeldt C, Dahm-Kähler P, Flöter

Rådestad A, *et al*. Primary treatment and relative survival by stage and age in vulvar squamous cell carcinoma: a population-based SweGCG study. Gynecologic Oncology. 2020; 159: 663–671.

[19] Rottmann M, Beck T, Burges A, Dannecker C, Kiechle M, Mayr D, *et al*. Trends in surgery and outcomes of squamous cell vulvar cancer patients over a 16-year period (1998–2013): a population-based analysis. Journal of Cancer Research and Clinical Oncology. 2016; 142: 1331–1341.

[20] Hami LT, Lampe B, Mallmann P, Forner DM. The impact of age on the prognosis of vulvar cancer. Oncology Research and Treatment. 2018; 41: 520–524.

[21] Prieske K, Woelber L, Muallem MZ, Eulenburg C, Jueckstock JK, Hilpert F, *et al*. Age, treatment and prognosis of patients with squamous cell vulvar cancer (VSCC)—analysis of the AGO-CaRE-1 study. Gynecologic oncology. 2021; 161: 442–448.

[22] Chen J, Ln H. A review of prognostic factors in squamous cell carcinoma of the vulva: evidence from the last decade. Seminars in Diagnostic Pathology. 2020. [Preprint].

[23] Zapardiel I, Iacoponi S, Coronado PJ, Zalewski K, Chen F, Fotopoulou C, *et al*. Prognostic factors in patients with vulvar cancer: the VULCAN study. International Journal of Gynecological Cancer. 2020; 30: 1285–1291

[24] Karataşlı V, Erkılınç S, Çakır İ, Can B, Karadeniz T, Gökçü M, *et al*. The effect of lymph node metastasis on overall survival and disease-free survival in vulvar cancer patients. Ginekologia Polska. 2020; 91: 62–67.

[25] Serre E, Diguisto C, Body G, Raimond E, Bendifallah S, Touboul C, *et al*. Prognostic significance of groin lymph node ratio in vulvar squamous cell carcinoma. Gynecologie, Obstetrique, Fertilite & Senologie. 2020; 48: 729–735.

[26] Eva LJ, Sadler L, Fong KL, Sahota S, Jones RW, Bigby SM. Trends in HPV-dependent and HPV-independent vulvar cancers: the changing face of vulvar squamous cell carcinoma. Gynecologic Oncology. 2020; 157: 450–455.

[27] Eva L, Sadler L, Thompson J, Sahota S, Fong KL, Jones RW, *et al*. HPV-independent and HPV-associated vulvar squamous cell carcinoma: two different cancers. International Journal of Gynecologic Cancer. 2022; 32: 1108–1114.

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