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Development and Validation of a Nomogram for Predicting Postoperative Distant Metastasis in Patients with Cervical Cancer

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Background: Cervical cancer is the fourth most commonly diagnosed malignant neoplasm among women worldwide. Despite improvements in treatment, the rate of postoperative metastasis remains a problem. Nomograms have been used to predict risk of tumor metastasis. We designed a nomogram to predict postoperative distant metastasis among cervical cancer patients, based on the SEER database, and estimated the performance of the nomogram by internal and external validations.

Material/Methods: We included 6421 participants and divided them into training (n=4495) and testing (n=1926) sets. Multivariate logistic regression was used to explore predictors. The nomogram's predictive value was assessed by internal (testing set) and external (561 Chinese patients) validations. The receiver operating characteristic curve (ROC) was plotted, and the area under the curve (AUC) value was calculated to evaluate the nomogram's discrimination. The nomogram's calibration was assessed via the Hosmer-Lemeshow test and calibration curve.

Results: Histologic type, T stage, treatment, tumor size, and positive lymph node were identified as independent predictors of postoperative distant metastasis in surgical patients ($P<0.05$). The developed nomogram had an AUC of 0.866 (95% CI: 0.844 to 0.888). The AUC and the chi-square for the Hosmer-Lemeshow test of the nomogram were 0.847 (95% CI: 0.807 to 0.888) and 11.292, respectively, ($P>0.05$) in the internal validation, and were 0.626 (95% CI: 0.548 to 0.704) and 316.53, respectively, ($P<0.05$) in the external validation.

Conclusions: Our nomogram showed a good predictive performance for postoperative distant metastasis in cervical cancer patients based on the SEER database. It remains to be determined if it is applicable to other populations.

Keywords: Database • Nomograms • Uterine Cervical Neoplasms • Validation Study

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Background

Cervical cancer is the fourth most commonly diagnosed malignant neoplasm among women worldwide [1]. It was estimated that 569 847 new cervical cancer cases and 311 365 deaths occur each year [2]. Despite significant improvements in the treatment of cervical cancer by surgical resection, the rate of postoperative distant metastasis remains an intractable problem, which has been proved to be associated with cervical cancer-related death [3,4]. Therefore, it is vital for physicians to be able to predict postoperative distant metastasis to improve the prognosis of cervical cancer patients.

Some predictors, such as pelvic lymph node metastasis [5], histologic type [6,7], and tumor size [8,9], have been revealed in previous studies to be associated with high risk of recurrence in patients with cervical cancer after surgical therapy. Several postoperative nomograms have been developed to predict the risk of recurrence in early-stage cervical cancer [10-13]. Moreover, Lee et al built a scoring system based on histologic type, the number of positive nodes, and surgical staging, which was used to assess the risk of distant recurrence in cervical cancer patients after radical surgery [14]. Although some investigations have focused on the predictive factors of distant metastasis in cervical cancer patients [15-17], scant evidence is available on models to predict the risk of distant metastasis after surgery in patients with cervical cancer. Je et al proposed a nomogram based on 1069 Korean patients with uterine cervical carcinoma undergoing postoperative radiotherapy to predict distant metastasis risks in 2014 [18], which was successfully validated among 109 cervical cancer patients from 3 branch hospitals of the Korea University Medical Center in 2017 [19]. Nomograms have been used to predict the possibility of tumor metastasis, and can visualize complex regression equations to make predictive results more intuitive and convenient for clinicians to use [20-22]. At present, no nomograms are available for other countries except Korea to predict the postoperative distant metastasis of cervical cancer.

In the present study, we constructed a clinical nomogram to predict postoperative distant metastasis among cervical cancer patients based on the Surveillance, Epidemiology, and End Results (SEER) database, and further estimated the predictive performance of the nomogram by internal and external validations.

Material and Methods

Data Sources and Study Design

The SEER database records information about demographics, primary tumor site, tumor morphology, stage at diagnosis, the first course of treatment, and vital status after follow-up for the US population. In this retrospective cohort study, data on cervical cancer cases were obtained from the SEER 18 Regs Custom Data (with additional treatment fields) of the National Cancer Institute (http://seer.cancer.gov/) between 2010 and 2016. The diagnosis of cervical cancer was confirmed through the International Classification of Diseases for Oncology, 3rd Edition (ICD-O-3), primary site codes C53.0, C53.1, C53.8, and C53.9, combined with histology codes, which are provided in **Supplementary Material**. Postoperative distant metastasis was defined through the cancer metastasis at distant site [CS met at DX, https://staging.seer.cancer.gov/cs/input/02.05.50/lung/mets/?(~view_schema~,~lung~)]. Furthermore, inclusion criteria were: (1) the age of patients was ≥18 years; (2) baseline data were complete; (3) patients were treated with surgery. Exclusion criteria were: (1) the tumor grade was unknown; (2) data on T and N stages were incomplete; (3) the tumor size was unknown; (4) information of tumor metastasis was missing.

Data Extraction

The following data were extracted from the SEER database: age at diagnosis, histologic type (squamous cell carcinoma, adenocarcinoma, adenosquamous carcinoma, and others), tumor grade, treatment (surgery, surgery+chemotherapy, surgery+radiotherapy, and surgery+radiotherapy+chemotherapy), T stage, N stage, tumor size, first malignant primary, regional nodes, regional nodes positive, and CS metastasis at DX. In this study, the outcome was postoperative distant metastasis, which was confirmed by the "CS mets at DX", with "Yes" suggesting the occurrence of postoperative distant metastasis.

Development and Validation of the Nomogram

To develop and validate the nomogram, all the enrolled patients were randomly divided into 2 sets by random number generation: training (n=4495) and testing (n=1926) sets. For the training set, factors that were statistically different between non-metastasis and metastasis groups through difference analysis were included in multivariate stepwise logistic regression analysis (rms package) to identify independent predictors for postoperative distant metastasis in patients with cervical cancer. Based on the identified predictors, the nomogram was constructed to predict postoperative distant metastasis for cervical cancer.

The testing set was utilized for interval validation of the nomogram, and external validation was conducted using clinical data from 561 Chinese cervical cancer patients who developed distant metastasis during postoperative follow-ups from the Meizhou People's Hospital between 3 February 2015 and 1 July 2020, which was approved by the Ethics Committee of the Meizhou People's Hospital (Huangtang Hospital), Meizhou

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Academy of Medical Sciences (2019-C-47). To further assess the applicability of the nomogram in the Chinese population, the nomogram's predictive ability was evaluated in subgroups stratified by age, histologic type, T stage, treatment, tumor size, and lymph node positivity. The receiver operating characteristic curve (ROC) was plotted, and the corresponding area under the curve (AUC) value (pROC package) was applied to evaluate the discrimination ability of the nomogram. Meanwhile, McNemar's test, Hosmer-Lemeshow test (ResourceSelection package), and calibration curve were used to assess the calibration of the nomogram.

Statistical Analysis

Each statistical test was two-sided, and $P<0.05$ was regarded as statistically significant. All statistical analysis was performed using SAS 9.4 software (SAS Institute, Cary, NC, USA) and R 4.0.2 software (R Foundation for Statistical Computing, Vienna, Austria). According to the SEER recommendations, data on cervical cancer patients of the corresponding ICD-O-3 codes were collected from the SEER with diagnosis year between 2010 and 2016, applying SEER*Stat 8.3.9 software (National Cancer Institute, Bethesda, MD, USA). Then, the TXT data file was exported, SAS 9.4 software was used to organize and split the training and testing sets, and statistical analysis was performed with R 4.0.2 software. Measurement data are presented as mean±standard deviation (Mean±SD) or median with quartile [M (Q_1, Q_3)], and the independent samples *t* test/Mann-Whitney U test was used for intergroup comparison. Count data are presented as the number of cases/constituent ratio [n (%)], and χ^2 test or Fisher's exact test was used for intergroup comparison.

Results

Baseline Characteristics

A total of 6421 patients were enrolled in this study, with 4495 patients in the training cohort and 1926 in the testing cohort. In the training cohort the average age was 47.15±12.42 years, and there were 2543 (56.57%) patients with squamous cell carcinoma, 783 (17.42%) patients with adenocarcinoma, 226 (5.03%) patients with adenosquamous carcinoma, and 943 (20.98%) patients with other histopathologic cell types. The tumor grades were: I (2033/45.23%), II (1486/33.06%), III (115/2.56%), and IV (861/19.15%). According to "SEER RESEARCH PLUS DATA DESCRIPTION CASES DIAGNOSED IN 1975-2018", cervical cancers have 4 tumor grades: Grade I (well differentiated), Grade II (moderately differentiated), Grade III (poorly differentiated), and Grade IV (undifferentiated). Of the 4495 patients in the training cohort, 2454 (54.59%) were treated with surgery only, 164 (3.65%) with surgery and chemotherapy, 482 (10.72%) with surgery and radiotherapy, and 1395 (31.03%) with surgery, radiotherapy, and chemotherapy. There were 190 (4.23%) patients with postoperative metastasis and 4305 (95.77%) without postoperative metastasis (**Figure 1, Table 1**).

Identification of Predictive Factors Based on the Training Set

Age, histologic type, tumor grade, number of lymph nodes, T stage, N stage, treatment, tumor size (≥4 cm), first malignant primary, and lymph node positivity were significantly different between patients with and without postoperative distant metastasis in the training set according to univariate analysis ($P<0.05$) (**Table 2**). However, only histologic type, T stage, treatment, tumor size, and positive lymph node were identified to be significantly associated with postoperative metastasis in multivariate analysis ($P<0.05$) (**Figure 2**).

Nomogram Construction and Evaluation

Based on the predictive factors, including histologic type, T stage, treatment, tumor size, and lymph node positivity, the prediction model was constructed: Y=-5.761+0.746×histologic type (adenosquamous carcinoma)+0.879×histologic type (other)+0.930× T stage (T2)+1.876× T stage (T3)+1.923× T stage (T4)+2.378× treatment (surgery and chemotherapy)+0.759× treatment (surgery and radiotherapy)+0.723× treatment (surgery, radiotherapy, and chemotherapy)+0.769× tumor size (≥4 cm)+1.272× lymph node positivity (yes). The nomogram prediction of postoperative distant metastasis was presented (**Figure 3**), with an AUC of 0.866 (95% CI: 0.844 to 0.888) (**Figure 4**). These results showed that the nomogram had good predictive ability in the training cohort.

Nomogram Validation

Internal and external validations were conducted to assess the predictive value of the nomogram. In the internal validation, the AUC for the predictive nomogram was 0.847 (95% CI: 0.807 to 0.888) (**Figure 5A**), and the chi-squares of the McNemar's and Hosmer-Lemeshow tests were 0.039 ($P>0.05$) and 11.292 ($P>0.05$), respectively (**Table 3**). Meanwhile, a calibration curve for the predictive nomogram was drawn in the internal validation cohort, indicating good calibration (**Figure 5B**). The results of internal validation indicated that the nomogram had good discrimination and calibration abilities. In the external validation, the AUC for the predictive nomogram was 0.626 (95% CI: 0.548 to 0.704) (**Figure 6A**), and the chi-squares of the McNemar's and Hosmer-Lemeshow tests were 111.484 ($P<0.05$) and 316.53 ($P<0.05$), respectively (**Table 4**). Meanwhile, a calibration curve for the predictive nomogram was drawn in the external validation cohort, indicating poor calibration (**Figure 6B**).

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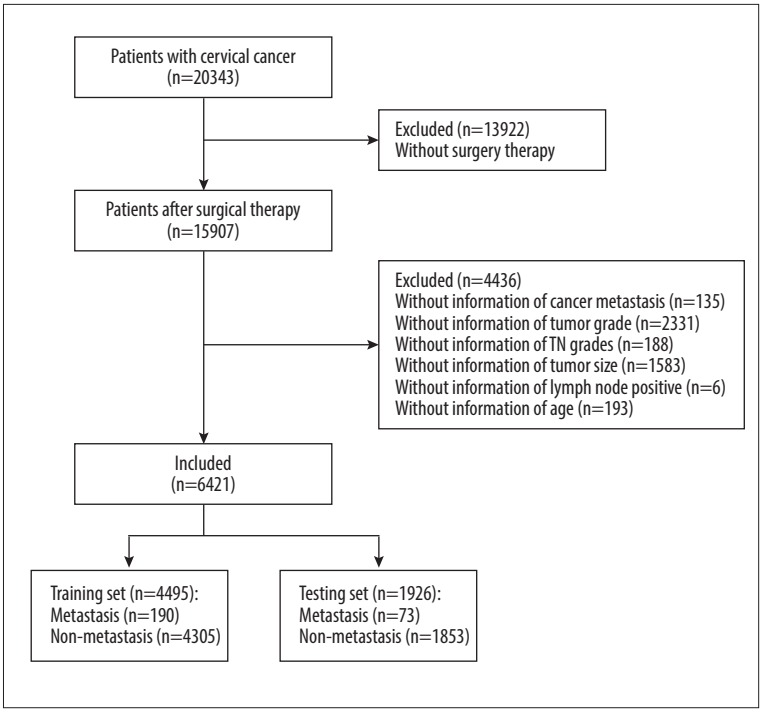

Figure 1. Flow chart for screening included patients with cervical cancer. Draw.io (version 12.6.5.330, JGraph Ltd.) was used for figure creation.

Table 1. Baseline characteristics of study populations [n (%)/M (Q_1, Q_3)].

Variables	Training set (n=4495)		Internal validation set (n=1926)	
Age at diagnosis (years), Mean±SD	47.15±12.42		46.63±12.29	
Histologic type, n (%)				
Squamous cell carcinoma	2543	(56.57)	1050	(54.52)
Adenocarcinoma	783	(17.42)	368	(19.11)
Adenosquamous carcinoma	226	(5.03)	93	(4.83)
Others	943	(20.98)	415	(21.55)
Grade, n (%)				
I	2033	(45.23)	827	(42.94)
II	1486	(33.06)	646	(33.54)
III	115	(2.56)	48	(2.49)
IV	861	(19.15)	405	(21.03)
Treatment, n (%)				
Surgery	2454	(54.59)	1012	(52.54)
Surgery + chemotherapy	164	(3.65)	66	(3.43)
Surgery + radiotherapy	482	(10.72)	211	(10.96)
Surgery + radiotherapy + chemotherapy	1395	(31.03)	637	(33.07)
CS met at DX, n (%)				
No	4305	(95.77)	1853	(96.21)
Yes	190	(4.23)	73	(3.79)

SD – standard deviation; CS met at DX – cancers metastasis at distant site.

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Table 2. Results of univariate analysis in the training set.

Variables	Training set		Statistics	*P*
	Non-metastasis (n=4305)	Metastasis (n=190)		
Age at diagnosis (years), Mean±SD	46.96±12.39	51.28±12.38	t=-4.700	<0.001
Histologic type, n (%)			χ^2=30.512	<0.001
Squamous cell carcinoma	2460 (57.14)	83 (43.68)		
Adenocarcinoma	758 (17.61)	25 (13.16)		
Adenosquamous carcinoma	209 (4.85)	17 (8.95)		
Other	878 (20.39)	65 (34.21)		
Grade, n (%)			Z=7.568	<0.001
I	1968 (45.71)	65 (34.21)		
II	1383 (32.13)	103 (54.21)		
III	104 (2.42)	11 (5.79)		
IV	850 (19.74)	11 (5.79)		
T stage, n (%)			Z=17.479	<0.001
T1	3552 (82.51)	65 (34.21)		
T2	616 (14.31)	67 (35.26)		
T3	115 (2.67)	46 (24.21)		
T4	22 (0.51)	12 (6.32)		
N stage, n (%)			χ^2=321.426	<0.001
N0	3645 (84.67)	65 (34.21)		
N1	660 (15.33)	125 (65.79)		
Treatment, n (%)			χ^2=328.799	<0.001
Surgery	2430 (56.45)	24 (12.63)		
Surgery+chemotherapy	118 (2.74)	46 (24.21)		
Surgery+radiotherapy	465 (10.80)	17 (8.95)		
Surgery+radiotherapy+chemotherapy	1292 (30.01)	103 (54.21)		
Tumor size (cm), n (%)			χ^2=175.142	<0.001
<4	3245 (75.38)	61 (32.11)		
≥4	1060 (24.62)	129 (67.89)		
First malignant primary, n (%)			χ^2=5.301	0.021
No	204 (4.74)	16 (8.42)		
Yes	4101 (95.26)	174 (91.58)		
Number of lymph node, M (Q_1, Q_3)	13.00 (0.00, 22.00)	5.00 (0.00, 16.00)	Z=-4.874	<0.001
Regional nodes positive, n (%)			χ^2=131.388	<0.001
No	2615 (60.74)	36 (18.95)		
Yes	1690 (39.26)	154 (81.05)		

SD – standard deviation; M – median.

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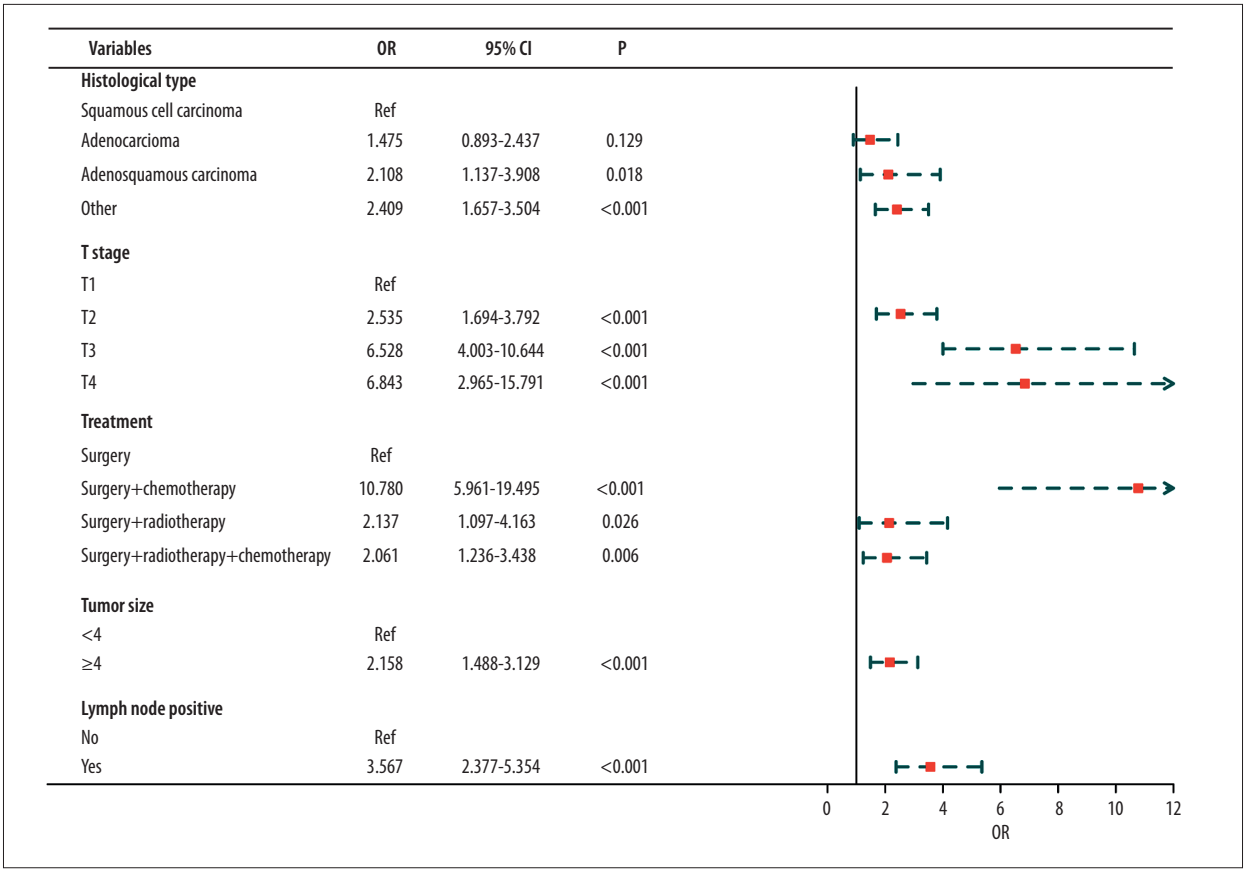

Figure 2. Results of multivariate analysis. R software (version 4.0.2, R Foundation for Statistical Computing) was used for figure creation.

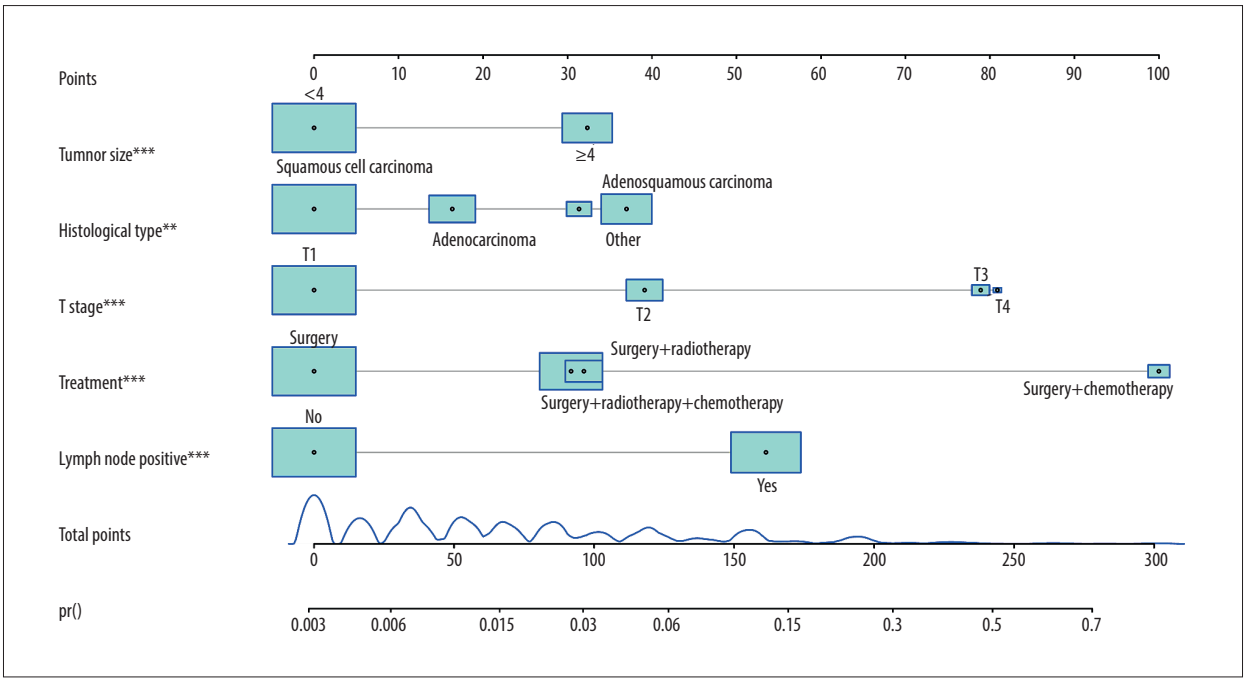

Figure 3. Nomogram prediction of postoperative metastasis. R software (version 4.0.2, R Foundation for Statistical Computing) was used for figure creation.

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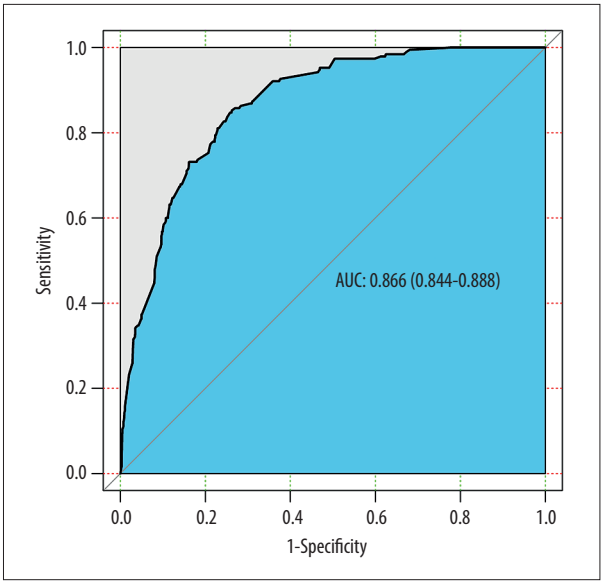

Figure 4. ROC curve of the predictive nomogram. R software (version 4.0.2, R Foundation for Statistical Computing) was used for figure creation.

These findings of the external validation suggested that the discrimination and calibration abilities of the nomogram were poor in the Chinese cohort. To further assess the applicability of the nomogram in the Chinese population, the nomogram's predictive ability was evaluated in subgroups stratified by age, histologic type, T stage, treatment, tumor size, and lymph node positivity. We found that the AUC of the nomogram for cervical cancer patients with adenocarcinoma was 0.811 (95% CI: 0.618 to 1.000) (**Table 5**). These results implied that the nomogram exhibited good performance in predicting postoperative distant metastasis among cervical cancer patients with adenocarcinoma.

Discussion

Early diagnosis and surgical treatment have been advocated for cervical cancer patients. However, the occurrence of postoperative distant metastasis remains a complex problem, and nomograms to accurately estimate postoperative distant metastasis for cervical cancer await more exploration. The present

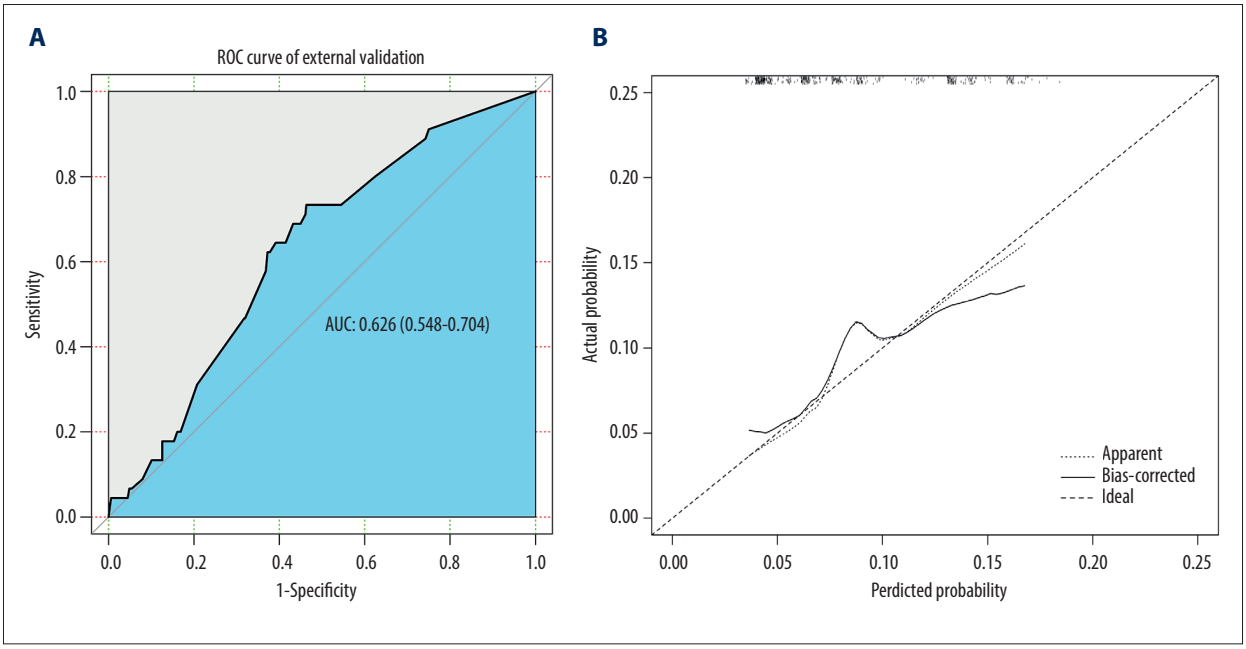

Figure 5. The (**A**) ROC curves and (**B**) calibration curve of the internal validation set. R software (version 4.0.2, R Foundation for Statistical Computing) was used for figure creation.

Table 3. Results of the McNemar's test in the internal validation set.

Predicted outcomes	Actual outcomes		McNemar	*P*
	Non-metastasis	Metastasis		
Non-metastasis	1802 (97.14)	53 (2.86)	χ^2=0.039	0.845
Metastasis	51 (71.83)	20 (28.17)		

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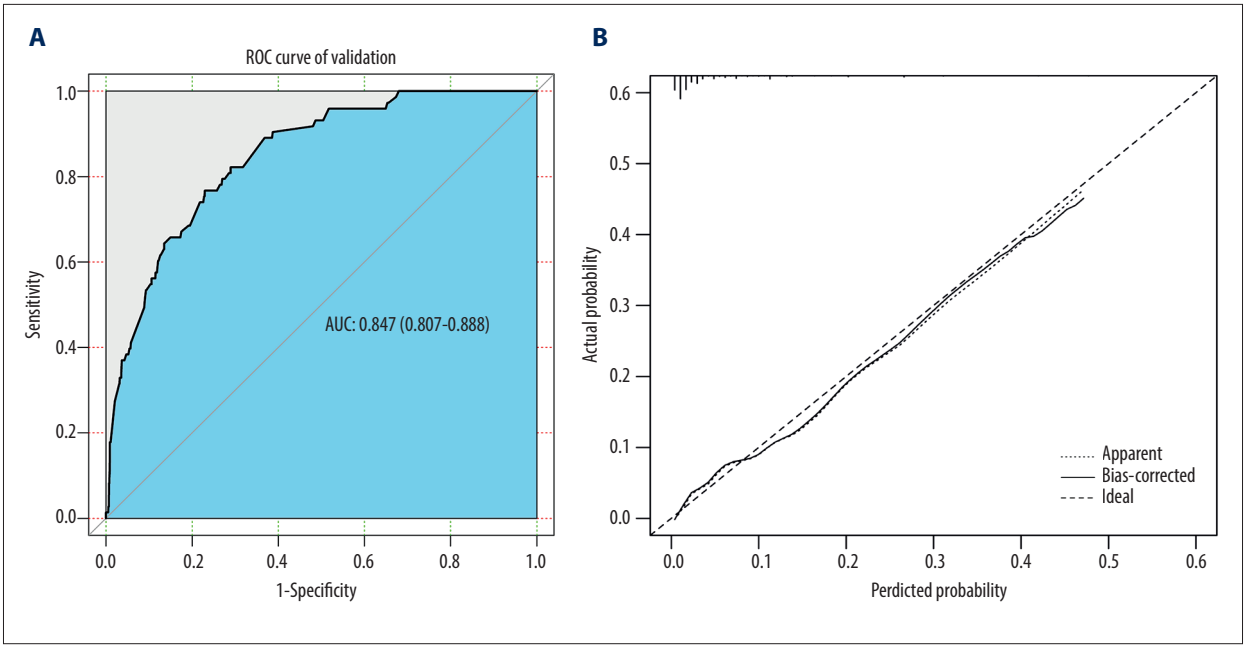

Figure 6. The (**A**) ROC curves and (**B**) calibration curve of the external validation set. R software (version 4.0.2, R Foundation for Statistical Computing) was used for figure creation.

Table 4. Results of the McNemar's test in the external validation set.

Predicted outcomes	Actual outcomes		McNemar	*P*
	Non-metastasis	Metastasis		
Non-metastasis	351 (94.35)	21 (5.65)	χ^2=111.484	<0.001
Metastasis	165 (87.30)	24 (12.70)		

study developed and validated a novel prediction tool for the risk of postoperative distant metastasis in cervical cancer patients. The selected predictive factors included histologic type, T stage, treatment, tumor size, and positive lymph node. Based on these predictors, a nomogram for predicting the risk of postoperative distant metastasis in cervical cancer patients was established, with an AUC of 0.866. In addition, the AUC of the nomogram was 0.847, with the chi-square for Hosmer-Lemeshow test of 11.292 (P>0.05) in the internal cohort, indicating very good predictive ability. However, the results of the external validation suggested that the discrimination and calibration abilities of the nomogram were poor in the Chinese cohort, while this nomogram had a good predictive ability for postoperative distant metastasis among cervical cancer patients with adenocarcinoma, as shown by subgroup analysis.

From the perspective of treatments, adjuvant treatment (including radiotherapy, chemotherapy, or radiotherapy combined with chemotherapy) would increase the risk of postoperative distant metastasis in cervical cancer patients. The chemotherapy agent is mainly used to act against tumor cells to shrink lesions. However, it can not only act on tumor cells but can also inhibit normal cells in other parts of the body to varying degrees, which causes damage to the body and induces a series of host reactions, forming a more suitable microenvironment for metastasis of malignant tumors. A previous review underscores the paradoxical pro-metastatic impacts of chemotherapy via remodeling of the primary tumor and generation of a favorable metastasis-promoting niche [23]. In addition, M2-type macrophages not only facilitate tumor growth and angiogenesis [24-26], but also promote tumor invasion and metastasis [27-30]. It has been reported that some chemotherapy drugs can induce monocytes to differentiate into M2-type macrophages by promoting the secretion of interleukin-6 and prostaglandin-2 in cervical cancer cells [31]. Ionizing radiation (IR) has been shown to promote tumor metastasis [32], and stimulate pro-metastatic cellular activities [33]. IR paradoxically facilitates metastasis and invasion of cancer cells via inducing epithelial-mesenchymal transition (EMT), hindering cancer management [34]. High-dose IR can induce endothelial cell dysfunction, but low-dose IR can promote the formation of capillaries by increasing the survival of endothelial

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Table 5. Results of subgroup analysis in the external validation set.

Variables	External validation set (n=561)	AUC (95% CI)
Age		
<60	463	0.655 (0.570-0.740)
≥60	98	0.504 (0.314-0.695)
Histologic type		
Squamous cell carcinoma	467	0.636 (0.553-0.718)
Adenocarcinoma	72	0.811 (0.618-1.000)
Adenosquamous carcinoma	9	NA
Others	13	0.636 (0.369-0.904)
T stage		
T1	361	0.598 (0.472-0.724)
T2	195	0.473 (0.352-0.594)
Treatment		
Surgery	245	0.670 (0.515-0.824)
Surgery+chemotherapy	11	0.639 (0.272-1.000)
Surgery+radiotherapy	183	0.537 (0.391-0.683)
Surgery+radiotherapy+chemotherapy	122	0.585 (0.450-0.720)
Tumor size		
<4	473	0.650 (0.562-0.737)
≥4	88	0.548 (0.285-0.812)
Regional nodes positive		
No	22	NA
Yes	538	0.630 (0.550-0.710)

AUC – area under the curve; CI – confidence interval; NA – not available.

cells induced by activation of the Akt-pathway, thus promoting tumor metastasis [35]. Administering vascular endothelial growth factor (VEGF) receptor-tyrosine kinase inhibitors immediately before IR exposure can prevent low-dose IR from promoting tumor growth and metastasis [36]. Beyond that, patients receiving surgery and chemotherapy or radiotherapy should have a regular follow-up after surgery.

Tumor size, T stage, and histologic type were independent predictors of postoperative distant metastasis in cervical cancer patients. A previous study indicated that a tumor size larger than 4 cm increased the risk of recurrence in cervical cancer patients [37]. Our results indicated that tumor size ≥4 cm was a predictor of increased distant metastasis in cervical cancer patients after surgery. Generally, a larger tumor with an adequate blood supply has longer growth time, increasing the possibility of lymph node metastasis, local infiltration, and distant metastasis, and the tumor can be prone to recurrence and distant metastasis after surgery. It has been proven that with the increase of tumor size, the number of tumor cells in the peripheral blood increases [38]. A study revealed that the number of tumor cells in bone marrow was positively correlated with tumor size in patients with cervical cancer [39]. From the perspective of the patients' condition, positive lymph node status was determined as an independent predictor of distant metastasis in cervical cancer patients after surgery. Lymph node metastasis has been confirmed to be a risk factor in cervical cancer patients who underwent surgery [40,41], which confirmed our result that lymph node positivity was a predictor of the increased risk of distant metastasis.

Although previous studies have developed several prediction models for the distant metastasis of cervical cancer, our research supplements these studies. Wang et al incorporated log of odds between the number of positive lymph nodes and the number of negative lymph nodes (LODDS) in establishing a prognostic nomogram for cervical cancer patients after surgery [42]. However, they focused on overall survival of patients with cervical cancer. In the present study, we specifically constructed a nomogram to predict postoperative distant metastasis of cervical cancer, with AUCs of 0.866 and 0.847 in the training and validation cohorts, respectively. Future studies

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can take LODDS into consideration for predicting postoperative distant metastasis among cervical cancer patients. A model to predict distant metastasis in cervical cancer patients was developed by Liu et al [43], and the differences between their model and our model are as follows. On the one hand, regarding subjects, cervical cancer patients treated with definitive radiotherapy were included in the study of Liu et al. Although radiotherapy has been recommended as a standard treatment for patients with advanced cervical cancer, most patients with cervical cancer undergo surgery, indicating that distant metastasis in many patients could not be predicted by the model constructed by Liu et al, while the nomogram we constructed could be applied to more patients. On the other hand, external validation that provides essential and robust evidence was performed to assess the application of the nomogram developed in our study. Further, Je et al proposed a nomogram in a multi-center Korean setting with 748 patients in the model development cohort and 321 in the external validation cohort, to predict postoperative distant metastasis for Korean patients with uterine cervical carcinoma. This model displayed an internally validated concordance index (C-index) of 0.71 and an externally validated C-index of 0.65 [18]. In 2017, the nomogram proposed by Je et al was subjected to external validation by Yoon et al in 109 Korean cervical cancer patients, showing with a C-index of 0.597 [19]. In the present study, apart from the lager sample size used for nomogram development, our nomogram was first developed and internally validated with the US population and externally verified in the Chinese population, which demonstrated an AUC of 0.847 in the internal validation and an AUC of 0.811 for cervical cancer patients with adenocarcinoma in the external validation, indicating great applicability of the nomogram to both the US population and the specific Chinese population. Moreover, Je et al's nomogram focused on the patients who received radiotherapy after surgery, whereas our nomogram focused on patients who underwent surgery only, surgery+chemotherapy, surgery+radiotherapy, and surgery+radiotherapy+chemotherapy, suggesting that our model can be used more widely. Lee et al also developed a scoring system among 223 node-positive cervical cancer patients from a single center in Korea to predict the risk of postoperative distant recurrence, with an internally validated C-index of 0.777 [14]. By contrast, the present study utilized nationally representative data in the US to establish the predictive nomogram, and then carried out external validation to asssess the performance of the model among Chinese patients in urgent need of postoperative distant metastasis prediction.

A strength of the present study is its relatively large sample size. Moreover, external validation of the predictive nomogram was carried out. However, our research indicated that the nomogram might not be applied to the Chinese population, possibly due to differences between Chinese and US populations. Our study also has several limitations. First, this was a retrospective study based on the SEER database. Second, the prediction model was validated in only 1 hospital. Patients from different institutions or ethnicities are needed to conduct external validations. Third, owing to the limited data collected, the effects of different surgical treatments and chemotherapy drugs on postoperative distant metastasis could not be evaluated, and further studies are required to explore the relationships between them.

Conclusions

Our nomogram had good predictive performance for postoperative distant metastasis in patients with cervical cancer based on 6421 participants from the SEER database, which may serve as a reference for clinicians to identify cervical cancer patients with a high risk of postoperative distant metastasis early to provide individualized therapy. However, whether the nomogram is applicable to other populations remains to be determined.

Declaration of figures' authenticity

All figures submitted have been created by the authors, who confirm that the images are original with no duplication and have not been previously published in whole or in part.

Supplementary Material

The diagnosis of cervical cancer was confirmed through the International Classification of Diseases for Oncology, 3rd Edition (ICD-O-3), primary site codes C53.0, C53.1, C53.8, C53.9, combined with histology codes 8000, 8001, 8010, 8012, 8013, 8015, 8020, 8022, 8033, 8041, 8042, 8045, 8046, 8050, 8051, 8052, 8070, 8071, 8072, 8073, 8074, 8075, 8076, 8082, 8083, 8084, 8094, 8098, 8120, 8123, 8130, 8140, 8144, 8200, 8210, 8240, 8244, 8246, 8255, 8260, 8261, 8262, 8263, 8310, 8313, 8323, 8380, 8382, 8384, 8410, 8441, 8460, 8461, 8480, 8481, 8482, 8490, 8500, 8542, 8560, 8570, 8574, 8720, 8800, 8801, 8802, 8805, 8890, 8896, 8900, 8910, 8912, 8920, 8931, 8933, 8935, 8950, 8963, 8980, 9044, 9080, 9100, 9110, 9473, 9581.

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