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Original Article

Nomogram model for predicting postoperative survival of patients with stage IB-IIA cervical cancer

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Abstract: To establish a prediction model based on clinical and pathological information for the long-term survival of patients with cervical cancer, we retrospectively analyzed the clinical data of patients pathologically diagnosed with stage IB-IIA cervical cancer between July 2007 and September 2017 in the Chinese Academy of Medical Sciences Cancer Hospital. Factors affecting the overall survival of the patients were analyzed using a Cox model, and a cervical cancer patient prediction nomogram model was established. A total of 2,319 patients were included in the study. According to the multivariate Cox regression analysis, number of complications, surgical methods, neoadjuvant treatment, lymph node metastasis, postoperative treatment, lymphovascular space invasion (LVSI), and other independent factors affecting prognosis were included to establish a nomogram. The nomogram consistency index in the training and validation cohorts was 0.691 and 0.615, respectively. The study established a highly accurate predictive model for the postoperative survival of cervical cancer patients.

Keywords: Nomogram model, cervical cancer, prognostic analysis, Cox analysis

Introduction

Cervical cancer is the second most common malignant tumor that threatens women's health. Global cancer statistics show that there are nearly 500,000 new cases each year, with an incidence rate of 16.2/100,000, and approximately 270,000 deaths per year, with a mortality rate of 9/100,000 [1]. With the popularization of physical examinations, an increasing number of patients are diagnosed in the early stages. Clinically, early cervical cancer (International Federation of Gynecology and Obstetrics [FIGO] 2014 stage, IB-IIA) is mainly treated via surgery, and the choice of postoperative adjuvant treatment is based on the pathological risk factors of patients [2]. For those with high-risk factors (lymph node metastasis, invasion of the uterus, and unclean cutting edge), concurrent chemoradiotherapy is selected; for those with medium risk factors (large-diameter tumor, deep muscle invasion, and intravascular tumor thrombus), adjuvant therapy is selected according to the Sedlis criteria. Although the guidelines recommend the above standardized treatment for stage IB-IIA cervical cancer, the prognosis of patients is quite different. The 5-year survival rate reported in the literature is 69%-90% [3]. Accurate assessment of patient prognosis is crucial to formulate individualized treatment and follow-up plans, and the establishment of an efficient prognostic assessment model is urgently needed. However, the prognostic evaluation models reported in the existing literature are not accurate or personalized [4-8].

The nomogram method fully integrates the various prognostic risk factors and quantifies them. Using this method, the prognostic score and survival probability of an individual can be obtained. Therefore, it is more accurate to establish a nomogram evaluation model to evaluate the prognosis. This method has been used to predict overall survival, disease-free survival, and the risk of delayed discharge after surgery in cases of metastatic urothelial tumors, thyroid cancer, and gynecological malignancies [9-12]. It has important value in estimating prognostic risk and designing individualized clinical program decisions and even clinical trials. However, an accurate nomogram

prognostic model for early cervical cancer has not yet been established.

Methods and materials

Participants

The medical records of patients with stage IB-IIA cervical cancer who underwent surgery at the Chinese Academy of Medical Sciences Cancer Hospital between July 2007 and September 2017 were analyzed. Preoperative biopsy confirmed the pathological diagnosis of cervical cancer. Preoperative examinations included tumor marker assessment; both computed tomography of the chest, abdomen, and pelvis and magnetic resonance imaging of pelvis to rule out distant metastases. In locally advanced cases (tumor size >4 cm), since it was challenging to directly perform surgery and 1-2 cycles of neoadjuvant chemotherapy were administered before surgery using the paclitaxel combined with platinum (cisplatin or carboplatin) regimen. Tumors shrunk to less than 4 cm before surgery. Patients accepted primary radical hysterectomy (Piver Type III or Q-M Type C) and pelvic lymph node dissection. Abdominal paraaortic lymph node dissection was performed when common iliac lymph nodes are positive or para-aortic lymph nodes are enlarged. All surgical patients were provided individualized postoperative treatment plans according to the postoperative pathological results and NCCN guidelines [13]. The above findings are based on the diagnosis and treatment conventions of early cervical cancer in our hospital. Lymph node metastasis was not included in the staging system, although lymph node metastasis is a significant prognostic factor, until the 2018 version FIGO stage. It was the first time that patients with pelvic and abdominal lymph node metastases were clearly defined as stage III. Due to the release of the new version of the staging, we adjusted the staging based on the actual situation of the patient according to the 2018 version of the FIGO staging system [14].

Inclusion and exclusion criteria

Inclusion: (i) Postoperative pathological diagnosis of primary cervical cancer, (ii) Stage IB-IIA according to the 2014 version of FIGO, (iii) Complete clinical information and follow-up information, (iv) Complete standard treatment.

Exclusion: (i) Follow-up time of less than 3 months, (ii) Incomplete clinical data.

Follow-up

The endpoint was five-year survival All patients received routine examinations after treatment every 3 months for the first 2 years, every 6 months for the following 3-5 years, and once a year thereafter. These included gynecological examination, vaginal stump smear cytology examination, imaging evaluation, and measurement of tumor markers. The deadline for follow-up was August 2020. The research protocol was approved by the Ethics Committee of the Cancer Hospital of the Medical Academy.

Statistical analysis

The patients were randomly divided into training and validation groups at a ratio of 7:3 using a table of random numbers. According to the World Health Organization (https://www.who.int/zh/news-room/fact-sheets/detail/women-s-health), age was classified into three groups (<45, 45-60, ≥60 years). Based on the number of cases of preoperative basic diseases (including hypertension, diabetes, lung dysfunction, asthma, chronic hepatitis, thrombosis, etc.), we used “None” to represent that the patient has no preoperative underlying disease, “1” to represent one preoperative underlying disease, and “2” to represent two and more than two preoperative underlying diseases. Tumor types were divided into squamous cell carcinoma, adenocarcinoma, adenosquamous carcinoma, and other types of tumors. We used “yes” or “no” to indicate the presence or absence of lymph node metastasis, radiotherapy, lymphovascular space invasion (LVSI), parauterine invasion, and vaginal margin. The 2018 FIGO staging, pathological differentiation, surgical methods (laparotomy and laparoscopy), interstitial invasion (≤1/2, >1/2), and tumor diameter (≤4 cm, >4 cm) were also divided into different groups. The squamous epithelial cell carcinogen (SCC) group was analyzed using the X-tile software to determine the best critical point. Categorical variables are expressed as counts and rates, while continuous variables are expressed as means and ranges. The comparison of rates between the two groups was performed using the chi-square test or Fisher’s exact test. Univariate and multivariate Cox regression analyses were used to determine

high-risk factors for the prognosis of cervical cancer, and hazard ratios (HRs) and 95% confidence intervals (95% CIs) were calculated. The statistical significance was set at P<0.05.

Nomogram establishment

Based on the results of multivariate Cox analysis in the training cohort, potential risk factors (P<0.05) were used to establish a nomogram using the "rms" package. The accuracy and calibration of the model were verified using the bootstrap verification method and consistency index (C-index). The closer the C-index to 1, the better the model discrimination. The closer the calibration curve of the graph calibration method to the standard curve (slope 1), the better the predictive ability of the nomogram. The R language software version used for the study was version 3.5.1.

Results

Clinical features and characteristics

A total of 2,319 eligible patients were included in the study, with a mean age of 45 years. Overall, 873 patients were aged <45 years, and 62 patients were aged ≥60 years. A total of 1,868 patients underwent laparotomy, and 88.53% had squamous cell carcinoma. Patients were classified according to the table of random numbers into the training group (n=123) and the validation group (n=696), and there was no significant difference between the two groups. The best cut-off point for SCC was 5.4 ng/mL, as determined using the X-tile software (3.6.1). Patients were regrouped according to the new FIGO 2018 guidelines. Some patients had their staging changed to stage IB3 owing to tumor diameters greater than 4 cm, while some were diagnosed with lymph node metastasis owing to preoperative imaging or postoperative pathology, leading to their stage being changed to IIIC; these patients were also included. Basic clinical and pathological information are shown in **Table 1**. The median follow-up duration was 74 months. There were no significant differences in age, body mass index, SCC, comorbidities, surgical methods, tumor diameter, tumor stage, tumor size, parauterine infiltration, interstitial infiltration, adjuvant therapy, follow-up time, recurrence, and death between the training and validation groups (P>0.05).

Cox regression survival analysis

Univariate Cox regression analysis showed that complications, surgical methods, histologic subtype, grade, SCC, lymph node metastasis, neoadjuvant chemotherapy, LVSI, and postoperative treatment (P<0.05) were factors related to prognosis. Multivariate regression analysis showed that preoperative complications (HR=2.581, P=0.025; two complications, HR=8.337, P=0.003), laparoscopy (HR=1.773, P=0.011), lymph node metastasis (HR=2.22, P<0.001), neoadjuvant chemotherapy (HR=1.816, P=0.002), LVSI (HR=1.522, P=0.04), and postoperative adjuvant radiotherapy (HR=1.752, P=0.03) were independent prognostic factors (**Table 2**). **Figure 1** shows the time survival curve based on patient complications, surgical methods, lymph node metastasis, neoadjuvant chemotherapy, LVSI, and postoperative treatment. The 5-year survival rate was 94.8% (Figure S1). Lymph node metastasis, neoadjuvant chemotherapy, LVSI, and postoperative treatment were all identified as prognostic factors (P<0.05). Although patient complications and surgical methods had no significant impact on patient survival, survival curve trends were also observed.

Nomogram prediction of all-cause mortality

Using the factors in the multivariate Cox regression, a nomogram was constructed (**Figure 2**). The C-index was 0.691 (95% CI: 0.6359-0.7462) in the training cohort and 0.6149 (95% CI: 0.5207-0.7092) in the validation cohort. The model was internally verified using the bootstrap verification method. The slopes of the calibration curves of the training group data set for 3 years and 5 years were 0.9322 and 0.9311, respectively, and the slopes of the validation group data set were 1.1856 and 0.9287, respectively (**Figure 3**). Within the actual range of results, the prediction accuracy of the model was good. When using the predictive model, the patient's pathological and therapeutic factors were included in the nomogram, and each influencing factor's value level was assigned according to the degree of contribution of each influencing factor in the model to the outcome variable (the size of the regression coefficient).

Table 1. Clinical characteristic of cervical cancer patients

Clinical features	All (N=2319)	Derivation Set (N=1623)	Validation (N=696)	*P* value
Age				
Mean	45	45	45	0.443
<45	1256 (54.161%)	873 (53.789%)	383 (55.029%)	
45-60	976 (42.087%)	688 (42.390%)	288 (41.379%)	
≥60	87 (3.752%)	62 (3.820%)	25 (3.592%)	
BMI (Median)	23.63	23.73	23.54	0.068
No. of patients with comorbidity				
None	2259 (97.413%)	1577 (97.166%)	682 (97.989%)	0.458
One	50 (2.156%)	39 (2.403%)	11 (1.580%)	
More than one	10 (0.431%)	7 (0.431%)	3 (0.431%)	
Surgical approach				0.447
Laparoscope	451 (19.448%)	309 (19.039%)	142 (20.402%)	
Laparotomy	1868 (80.552%)	1314 (80.961%)	554 (79.598%)	
Tumor size (cm)	3.5	3.5	3.5	0.587
Histologic subtype				0.397
Squamous cell carcinoma	2053 (88.530%)	1429 (88.047%)	624 (89.655%)	
Adenocarcinoma	221 (9.530%)	159 (9.797%)	62 (8.908%)	
Adenosquamous carcinoma	45 (1.940%)	35 (2.157%)	10 (1.437%)	
Stage				0.781
IB1	260 (11.212%)	184 (29.535%)	76 (10.920%)	
IB2	837 (36.093%)	594 (36.599%)	243 (34.914%)	
IB3	361 (15.567%)	245 (15.096%)	116 (16.667%)	
IIA1	211 (9.099%)	144 (8.872%)	67 (9.626%)	
IIA2	134 (5.778%)	94 (5.792%)	40 (5.747%)	
IIIC1	492 (21.216%)	348 (21.442%)	144 (20.690%)	
IIIC2	24 (1.035%)	14 (0.823%)	10 (1.437%)	
Grade				0.251
Low	1213 (52.307%)	858 (52.865%)	355 (51.006%)	
Median	898 (38.724%)	612 (37.708%)	286 (41.092%)	
High	148 (6.382%)	110 (6.778%)	38 (5.460%)	
Others	60 (2.587%)	43 (2.649%)	17 (2.443%)	
SCC	1.6	1.6	1.5	0.092
LNM				0.057
YES	431 (18.586%)	318 (19.593%)	113 (16.236%)	
NO	1888 (81.414%)	1305 (80.407%)	583 (83.764%)	
Positive margin				0.354
YES	2 (0.086%)	2 (0.123%)	0	
NO	2317 (99.914%)	1621 (99.877%)	696 (100%)	
Parametrial infiltration				0.928
YES	24 (1.035%)	17 (1.047%)	7 (1.006%)	
NO	2295 (98.965%)	1606 (98.953%)	689 (98.994%)	
LVSI				0.537
YES	677 (29.194%)	499 (30.746%)	197 (28.305%)	
NO	1642 (70.806%)	1143 (69.871%)	480 (68.966%)	
Interstitial infiltration				0.86
≤1/2	1303 (56.188%)	910 (56.069%)	393 (56.466%)	
>1/2	1016 (43.812%)	713 (43.931%)	303 (43.534%)	

NACT				0.231
YES	696 (30.013%)	483 (29.760%)	190 (27.299%)	
NO	1623 (69.987%)	1140 (70.240%)	506 (72.701%)	
Radiotherapy				0.717
YES	186 (8.021%)	128 (7.887%)	58 (8.333%)	
NO	2133 (91.979%)	1495 (92.113%)	638 (91.667%)	
Chemotherapy				0.636
YES	272 (11.729%)	187 (11.522%)	85 (12.213%)	
NO	2047 (88.271%)	1436 (88.478%)	611 (87.787%)	
Chemoradiotherapy				0.328
YES	1042 (44.933%)	740 (45.595%)	302 (43.391%)	
NO	1277 (55.066%)	883 (54.405%)	394 (56.609%)	
Recurrence				0.096
YES	245 (10.565%)	183 (11.275%)	62 (8.908%)	
NO	2074 (89.435%)	1440 (88.725%)	634 (91.092%)	
Death				0.138
YES	154 (6.641%)	116 (7.147%)	38 (5.460%)	
NO	2165 (93.359%)	1507 (92.823%)	658 (94.504%)	
Median follow-up time (month)	74	75 (4.621%)	73.5	0.497

LVSI, lymphovascular space invasion; BMI, body mass index; NACT, neoadjuvant chemotherapy; SCC, squamous epithelial cell carcinogen; LNM, lymph node metastasis.

Table 2. Univariate and multivariate analyses of OS in the derivation set

Variable	Univariate				Multivariate			
	HR	95% CI		*P* value	HR	95% CI		*P* value
Age								
Mean (median)								
<45	1	--	--	--				
45-60	1.146	0.79	1.66	0.473				
≥60	1.041	0.378	2.868	0.938				
BMI≥23.2, N (%)	1.146	0.797	1.65	0.462				
No. of patients with comorbidity								
None	1	--	--	--	1	--	--	--
One	2.422	1.063	5.515	0.035	2.581	1.126	5.916	0.025
Two or more	4.635	1.144	18.788	0.032	8.337	2.030	34.239	0.003
Surgical approach								
Laparotomy	1	--	--	--	1	--	--	--
Laparoscope	1.743	1.132	2.684	0.012	1.773	1.142	2.753	0.011
Tumor size >4 (cm)	1.222	0.829	1.8	0.312				
Histologic subtype								
Squamous cell carcinoma	1	--	--	--				
Adenocarcinoma	1.176	0.646	142	0.596				
Adenosquamous carcinoma	2.51	1.1	5.73	0.029				
Stage								
IB1	1	--	--	--				
IB2	1.606	0.754	3.42	0.22				
IB3	1.816	0.795	4.149	0.157				
IIA1	1.766	0.71	4.39	0.221				
IIA2	1.834	0.665	5.059	0.241				

IIIC1	1.905	0.871	4.167	0.107				
IIIC2	<0.001	<0.001	4.724	0.952				
Grade								
Low	1	--	--	--				
Median	0.563	0.373	0.851	0.006				
High	0.64	0.295	1.39	0.26				
Others	0.24	0.033	1.693	0.151				
Initial treatment SCC	2.064	1.159	2.545	<0.001				
≤5.4	1	--	--	--				
>5.4	2.064	1.159	2.545	<0.001				
LNM								
NO	1	--	--	--	1	--	--	--
YES	2.86	1.974	4.144	<0.001	2.22	1.495	3.296	<0.001
Vaginal margin								
NO	1	--	--	--				
YES	0.05	<0.001	>100	0.817				
Parametrial infiltration								
NO	1	--	--	--				
YES	0.754	0.105	5.4	0.779				
LVSI								
NO	1	--	--	--	1	--	--	--
YES	1.919	1.325	2.778	0.001	1.522	1.020	2.270	0.04
Interstitial infiltration								
NO	1	--	--	--				
YES	1.204	0.836	1.734	0.318				
NACT								
NO	1	--	--	--	1	--	--	--
YES	1.725	1.19	2.5	0.004	1.816	1.242	2.656	0.002
Postoperative treatment								
Radiotherapy	4,254	2.3	7.862	<0.001	3.229	1.729	6.030	--
Chemotherapy	1.467	0.711	3.026	0.3	1.338	0.645	2.778	0.434
Chemoradiotherapy	2.33	1.435	3.782	0.001	1.752	1.055	2.908	0.03

LVSI, lymphovascular space invasion; BMI, body mass index; NACT, neoadjuvant chemotherapy; SCC, squamous epithelial cell carcinogen; LNM, lymph node metastasis; CI, confidence interval; HR, hazard ratio.

The scores were then summed to obtain the total score, and the predicted value of the individual outcome event was calculated through the function relationship between the total score and the probability of the outcome event. For example, a 55-year-old patient with cervical cancer with high blood pressure, with no neoadjuvant chemotherapy, receiving laparoscopic surgery, with moderately differentiated postoperative pathology and stage IB1, no lymph node metastasis, no LVSI, and no need for adjuvant treatment after surgery will have a score of 82 points, with 3-year, 5-year, and 10-year survival probabilities of 91.89%, 89.74%, and 80.79%, respectively.

Discussion

We established a single-center cervical cancer database of patients with stage IB-IIA cervical cancer who underwent surgery at the Chinese Academy of Medical Sciences Cancer Hospital between July 2007 and September 2017. The predictive indicators included complications, surgical methods, lymph node metastasis, neoadjuvant chemotherapy, LVSI, and postoperative treatment, as well as verification of our nomogram, which showed good prediction accuracy. Accurate prediction of the prognosis of patients with early cervical cancer is crucial for providing appropriate consultation, condi-

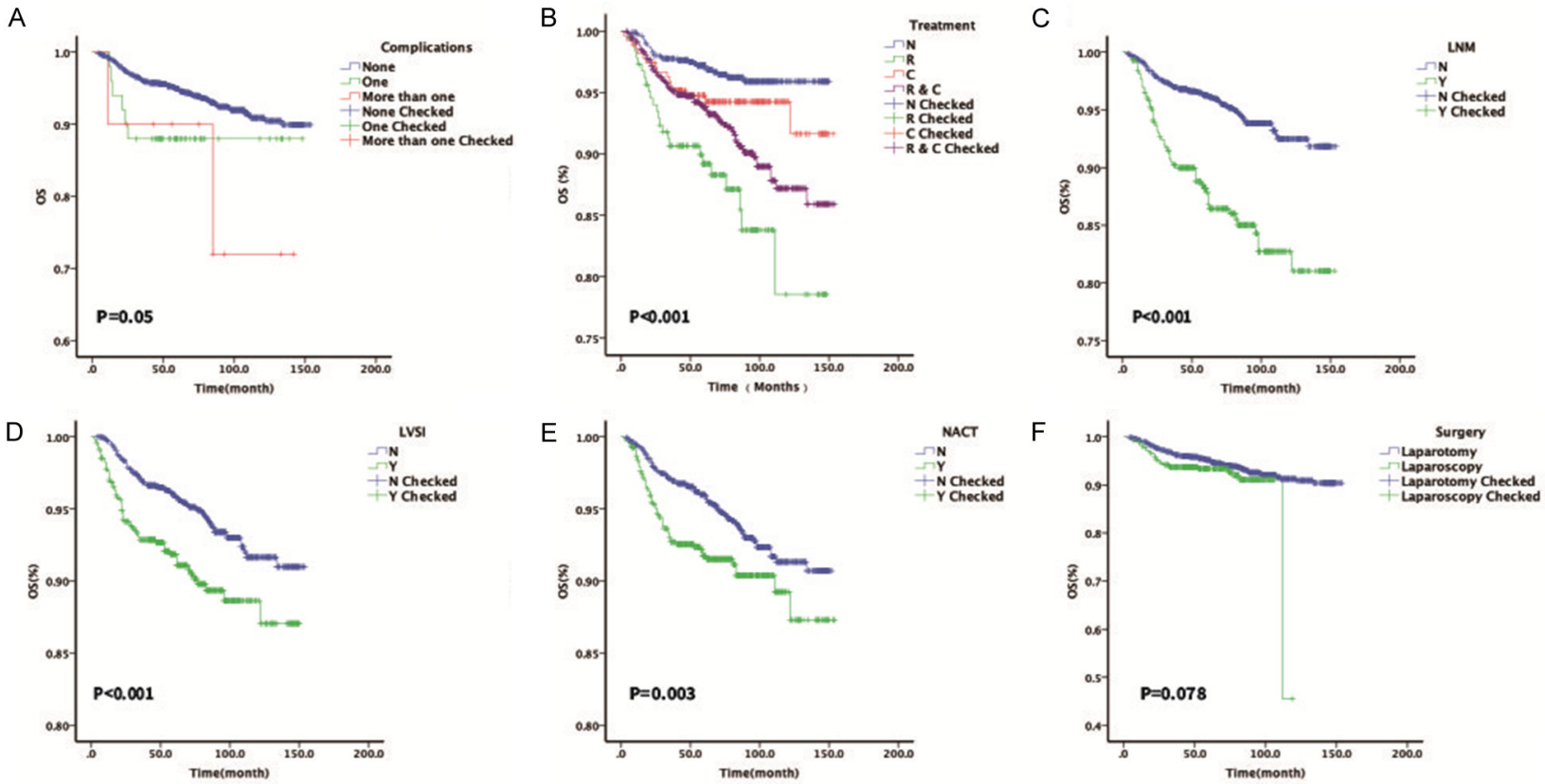

Figure 1. The time survival curve divided by groups according to the influencing factors. A. Kaplan-Meier curves demonstrating OS by survival in months based on comorbidity. B. Kaplan-Meier curves demonstrating OS by survival in months based on treatment. C. Kaplan-Meier curves demonstrating OS by survival in months based on lymph node metastasis. D. Kaplan-Meier curves demonstrating OS by survival in months based on LVSI. E. Kaplan-Meier curves demonstrating OS by survival in months based on NACT. F. Kaplan-Meier curves demonstrating OS by survival in months based on surgery. LNM: lymph node metastasis; NACT: neoadjuvant chemotherapy; LVSI: lymphatic vascular space invasion; OS, overall survival.

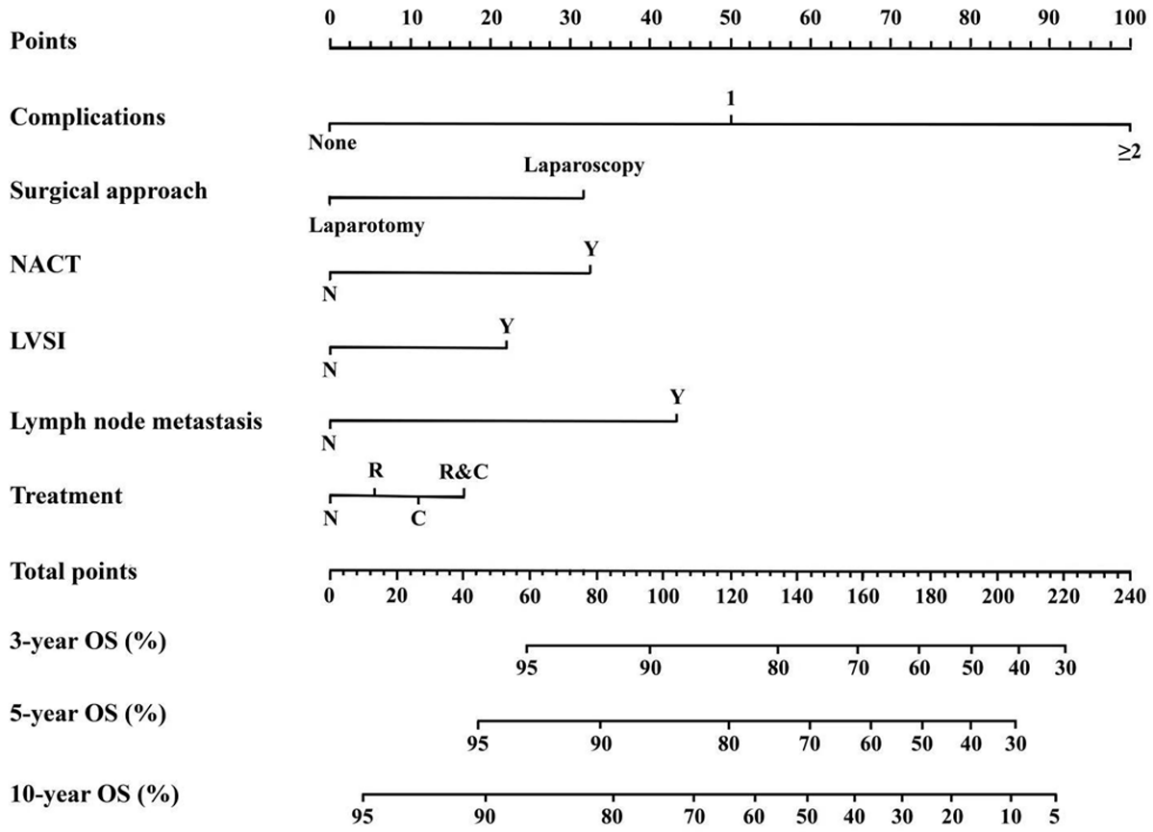

Figure 2. Nomogram for predicting survival rate of cervical cancer. NACT: neoadjuvant chemotherapy; LVSI: lymphatic vascular space invasion; OS, overall survival.

tion notification, diagnosis and treatment planning, and follow-up programs. At present, several prediction models related to cervical cancer have been established, and each has advantages and disadvantages. In the studies by Wang et al. [15] and Zhang et al. [16], the Surveillance, Epidemiology, and End Results database was used to establish the nomogram model with good prediction accuracy, but the data used were incomplete and belonged to several institutions; furthermore, the treatment process and standards were difficult to control. Huang et al. [17] used the FIGO stage, lymph node metastasis, and systemic immune inflammation indicators to establish a nomogram to predict the 3-year and 5-year survival rates of cervical cancer patients, but the model was not verified and only three factors were included, leading to large errors in prediction in some extreme cases. Varol Gulseren et al. [18] and Polterauer et al. [19] established a cervical cancer nomogram prediction model that achieved high prediction accuracy; however, the sample size was small. The representativeness of the model may require larger samples for testing.

In view of the above problems, we established a nomogram based on a real-world case review to predict the survival rate of cervical cancer patients, aiming to provide individualized and accurate prognosis for patients. The data of this nomogram were obtained from many clinical cases rather than a database; thus, the included predictors are more comprehensive. This study was conducted on patients with postoperative pathological diagnosis of stage IB-IIA, focusing on a more specific subset of patients with cervical cancer. At the same time, compared with other multicenter and database-based research results, single-center source data have characteristics of high consistency and standardized treatment methods. This eliminates the differences in surgical methods and technical and personal judgment standards of surgeons and pathologists in many institutions, as well as in many countries, to reduce the interference of human factors

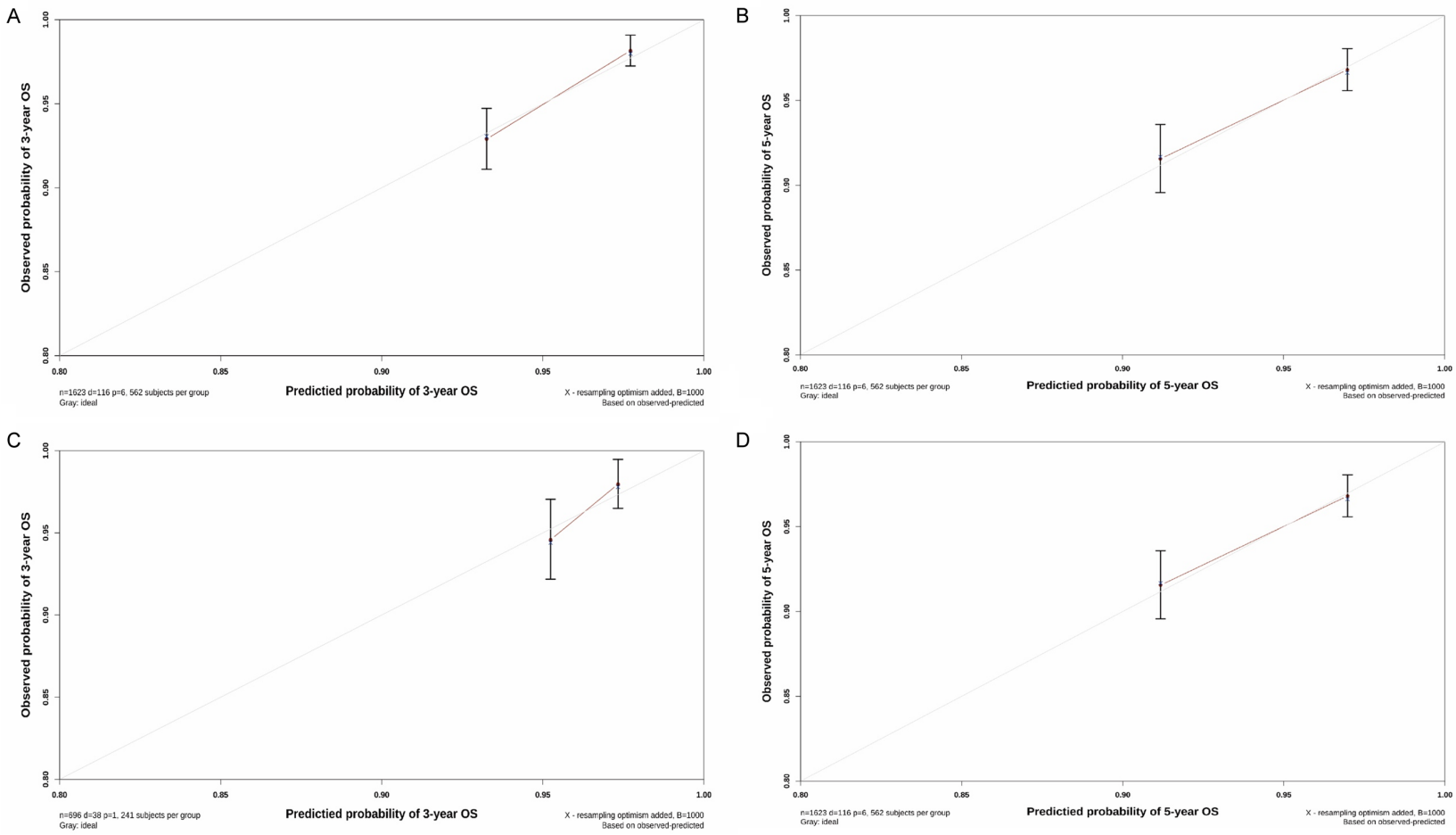

Figure 3. Calibration curve. A. The 3-year survival rate of the training group was predicted using the nomogram correction curve. B. The 5-year survival rate of the training group was predicted using the nomogram correction curve. C. The 3-year survival rate of the validation group was predicted using the nomogram correction curve. D. The 5-year survival rate of the validation group was predicted using the nomogram correction curve.

on the research results and highlight the influence of various clinical and pathological factors on prognosis. This study involves a cervical cancer prediction model with the largest sample recruited from a single center and includes several clinical variables. On this basis, the C-index of the model still reaches a level similar to that in other studies [19]; therefore, its representativeness and persuasiveness are worthy of recognition. Moreover, the factors included in the nomogram, such as operation mode, patients' chronic disease, and lymph node metastasis, are more innovative than those in previous prediction models.

This study innovatively incorporated laparotomy and laparoscopic surgery into the nomogram model because it was found that laparoscopic surgery is a factor influencing the prognosis of cervical cancer. This conclusion is also consistent with the conclusions of prospective studies in some large cases [20-22]. At present, the mainstream view still believes that laparoscopy is a risk factor for unfavorable prognosis in patients with cervical cancer. It is believed that the pneumoperitoneum environment, use of uterine manipulators, level of operation proficiency, and lack of tumor-free technology have led to poor prognosis [23, 24]. At present, cervical cancer patients who choose laparoscopic surgery should be strictly informed of the indications and the benefits and risks. In this study, the influencing factor of laparoscopy was included in the nomogram model, providing a reference for patients and doctors to discuss when choosing surgical methods.

Innovatively, patients' own chronic disease conditions were added to the prediction model. The patient's other chronic diseases is also an important factor that affects the prognosis of tumors. Previous studies have also indicated that approximately 11.2% of esophageal cancer patients and 11.8% of head and neck cancer patients die of non-tumor factors [25, 26]. It is believed that this phenomenon also exists in cervical cancer, but this factor is often not considered when assessing the overall survival rate of cancer patients. This study included patients' own chronic diseases before surgery, which can more accurately predict the patient's overall risk of death. We should pay attention to patients with chronic diseases alongside tumor conditions. During the preoperative evaluation, comprehensive consideration of the benefits that patients may obtain through surgery and active treatment of chronic diseases may be of great significance in improving the prognosis of patients.

Lymph node metastasis is a poor prognostic factor for many tumors, but its role has not been reflected in previous cervical cancer staging. Until the 2018 version of the new FIGO staging of cervical cancer, the presence of positive lymph nodes was classified as stage III. Our research results fully confirmed the impact of lymph node metastasis on the prognosis of patients, and the inclusion of lymph node metastasis in the survival prediction model can more accurately reflect the prognosis of patients.

In the latest FIGO staging, although LVSI does not affect staging, it is a high-risk factor for recurrence in cervical cancer with a tumor diameter of <4 cm. Postoperative adjuvant radiotherapy is recommended for improving the local recurrence rate [14, 27, 28]. Some studies suggest that LVSI should be combined with lymph node metastasis to evaluate the prognosis of patients [27]. In our study, LVSI was an independent prognostic factor for patients with cervical cancer, the positive rate of LVSI was 28.5%, and the prognosis of LVSI-positive patients was significantly worse than that of LVSI-negative patients. Therefore, we included LVSI in the prognosis prediction model, which is conducive to the accuracy of this nomogram model in predicting the survival of patients and guiding the individualized treatment of patients after surgery.

In this study, 21.55% of patients receiving neoadjuvant chemotherapy were in stage IIIC, and 23.64% were in stage IB3 or IIA2. Large lymph node metastasis and tumor diameter may affect patient prognosis. The value of neoadjuvant chemotherapy remains controversial [27].

Although we successfully established a model that could accurately predict individual prognosis, there remain some limitations. First, this study uses single-center data analysis; hence, data from high-level medical institutions with strict and uniform treatment standards and programs and unified follow-up and review requirements are required to test and verify our model. On this premise, a multicenter prospective study is needed to increase the number of

cases to further improve the accuracy and representativeness of the prediction model. In addition, this study did not include information on the gene targets and molecular markers. The specific biological characteristics of cervical cancer cannot be fully described based on its pathological and clinical characteristics. Molecular biology, genetics, and epigenetics provide new evaluation indicators of individual cancer potential behavior [29, 30]. Therefore, new biomarkers should be added to future prediction models to provide more accurate individual risk estimations. Considering this, the nomogram prediction model established in this study can be used as a basis for future research.

Disclosure of conflict of interest

None.

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References

[1] Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J and Jemal A. Global cancer statistics, 2012. CA Cancer J Clin 2015; 65: 87-108.

[2] FIGO Committee on Gynecologic Oncology. FIGO staging for carcinoma of the vulva, cervix, and corpus uteri. Int J Gynaecol Obstet 2014; 125: 97-98.

[3] Saatli B, Olgan S, Gorken IB, Uslu T, Saygili U, Dicle N, Cingillioglu B, Gumurdulu D, Guzel AB and Koyuncuoglu M. Tumor-free distance from outermost layer of cervix is of prognostic value in surgically treated cervical cancer patients: a multicenter study. Arch Gynecol Obstet 2014; 289: 1331-1335.

[4] Sakakibara A, Matsui K, Katayama T, Higuchi T, Terakawa K and Konishi I. Age-related survival disparity in stage IB and IIB cervical cancer patients. J Obstet Gynaecol Res 2019; 45: 686-694.

[5] Yokoi E, Mabuchi S, Takahashi R, Matsumoto Y, Kuroda H, Kozasa K and Kimura T. Impact of histological subtype on survival in patients with locally advanced cervical cancer that were treated with definitive radiotherapy: adenocarcinoma/adenosquamous carcinoma versus squamous cell carcinoma. J Gynecol Oncol 2017; 28: e19.

[6] Kose MF, Kiseli M, Kimyon G, Ocalan R, Yenen MC, Tulunay G, Turan AT, Ureyen I and Boran N. Extraperitoneal lymph node dissection in locally advanced cervical cancer; the prognostic factors associated with survival. J Turk Ger Gynecol Assoc 2017; 18: 77-84.

[7] Gai J, Wang X, Meng Y, Xu Z, Kou M and Liu Y. Clinicopathological factors influencing the prognosis of cervical cancer. J BUON 2019; 24: 291-295.

[8] Je HU, Han S, Kim YS, Nam JH, Park W, Song S, Song C, Kim JH, Kim J, Yoon WS, Yoon MS, Choi HJ and Kim JY. Risk prediction model for disease-free survival in women with early-stage cervical cancers following postoperative (chemo)radiotherapy. Tumori 2018; 104: 105-110.

[9] Apolo AB, Ostrovnaya I, Halabi S, Iasonos A, Philips GK, Rosenberg JE, Riches J, Small EJ, Milowsky MI and Bajorin DF. Prognostic model for predicting survival of patients with metastatic urothelial cancer treated with cisplatin-based chemotherapy. J Natl Cancer Inst 2013; 105: 499-503.

[10] Iasonos A, Schrag D, Raj GV and Panageas KS. How to build and interpret a nomogram for cancer prognosis. J Clin Oncol 2008; 26: 1364-1370.

[11] Lang BH and Wong CK. Validation and comparison of nomograms in predicting disease-specific survival for papillary thyroid carcinoma. World J Surg 2015; 39: 1951-1958.

[12] Penn CA, Kamdar NS, Morgan DM, Spencer RJ and Uppal S. Preoperatively predicting non-home discharge after surgery for gynecologic malignancy. Gynecol Oncol 2019; 152: 293-297.

[13] Abu-Rustum NR, Yashar CM, Bean S, Bradley K, Campos SM, Chon HS, Chu C, Cohn D, Crispens MA, Damast S, Fisher CM, Frederick P, Gaffney DK, Giuntoli R, Han E, Huh WK, Lurain Iii JR, Mariani A, Mutch D, Nagel C, Nekhlyudov L, Fader AN, Remmenga SW, Reynolds RK, Sisodia R, Tillmanns T, Ueda S, Urban R, Wyse E, McMillian NR and Motter AD. NCCN guidelines insights: cervical cancer, version 1.2020. J Natl Compr Canc Netw 2020; 18: 660-666.

[14] Bhatla N, Aoki D, Sharma DN and Sankaranarayanan R. Cancer of the cervix uteri. Int J Gynaecol Obstet 2018; 143 Suppl 2: 22-36.

[15] Wang C, Yang C, Wang W, Xia B, Li K, Sun F and Hou Y. A prognostic nomogram for cervical cancer after surgery from SEER database. J Cancer 2018; 9: 3923-3928.

[16] Zhang S, Wang X, Li Z, Wang W and Wang L. Score for the overall survival probability of patients with first-diagnosed distantly metastatic cervical cancer: a novel nomogram-based risk assessment system. Front Oncol 2019; 9: 1106.

[17] Huang H, Liu Q, Zhu L, Zhang Y, Lu X, Wu Y and Liu L. Prognostic value of preoperative systemic immune-inflammation index in patients with cervical cancer. Sci Rep 2019; 9: 3284.
[18] Gulseren V, Kocaer M, Cakir I, Ozdemir IA, Sanci M and Gungorduk K. Postoperative nomogram for the prediction of disease-free survival in lymph node-negative stage I-IIA cervical cancer patients treated with radical hysterectomy. J Obstet Gynaecol 2019; 40: 699-704.
[19] Polterauer S, Grimm C, Hofstetter G, Concin N, Natter C, Sturdza A, Potter R, Marth C, Reinthaller A and Heinze G. Nomogram prediction for overall survival of patients diagnosed with cervical cancer. Br J Cancer 2012; 107: 918-924.
[20] Melamed A and Ramirez PT. Changing treatment landscape for early cervical cancer: outcomes reported with minimally invasive surgery compared with an open approach. Curr Opin Obstet Gynecol 2020; 32: 22-27.
[21] Ramirez PT, Frumovitz M, Pareja R, Lopez A, Vieira M, Ribeiro R, Buda A, Yan X, Shuzhong Y, Chetty N, Isla D, Tamura M, Zhu T, Robledo KP, Gebski V, Asher R, Behan V, Nicklin JL, Coleman RL and Obermair A. Minimally invasive versus abdominal radical hysterectomy for cervical cancer. N Engl J Med 2018; 379: 1895-1904.
[22] Cusimano MC, Baxter NN, Gien LT, Moineddin R, Liu N, Dossa F, Willows K and Ferguson SE. Impact of surgical approach on oncologic outcomes in women undergoing radical hysterectomy for cervical cancer. Am J Obstet Gynecol 2019; 221: 619.e1-619.e24.
[23] Koninckx PR, Puga M, Ussia A, Zupi E, Keckstein J, Adamian L, Solima E and Wattiez A. Regarding: "the LACC trial and minimally invasive surgery in cervical cancer". J Minim Invasive Gynecol 2020; 27: 239-240.
[24] Melamed A, Margul DJ, Chen L, Keating NL, Del Carmen MG, Yang J, Seagle BL, Alexander A, Barber EL, Rice LW, Wright JD, Kocherginsky M, Shahabi S and Rauh-Hain JA. Survival after minimally invasive radical hysterectomy for early-stage cervical cancer. N Engl J Med 2018; 379: 1905-1914.
[25] Yu X, Gao S, Xue Q, Tan F, Gao Y, Mao Y, Wang D, Zhao J, Li Y, He J and Mu J. Development of a predictive nomogram for cause-specific mortality in surgically resected early-stage oesophageal cancer: a surveillance, epidemiology, and end results (SEER) analysis. J Thorac Dis 2020; 12: 2583-2594.
[26] Shen W, Sakamoto N and Yang L. Cause-specific mortality prediction model for patients with basaloid squamous cell carcinomas of the head and neck: a competing risk analysis. J Cancer 2018; 9: 4009-4017.
[27] Wang JD, Kong WM and Jiang H. FIGO 2018 staging of cervical cancer and related issues. Zhonghua Zhong Liu Za Zhi 2020; 42: 94-98.
[28] Matsuo K, Machida H, Mandelbaum RS, Konishi I and Mikami M. Validation of the 2018 FIGO cervical cancer staging system. Gynecol Oncol 2019; 152: 87-93.
[29] Qin S, Gao Y, Yang Y, Zhang L, Zhang T, Yu J and Shi C. Identifying molecular markers of cervical cancer based on competing endogenous rna network analysis. Gynecol Obstet Invest 2019; 84: 350-359.
[30] Wang H, Li SW, Li W and Cai HB. Elastic net-based identification of a multigene combination predicting the survival of patients with cervical cancer. Med Sci Monit 2019; 25: 10105-10113.

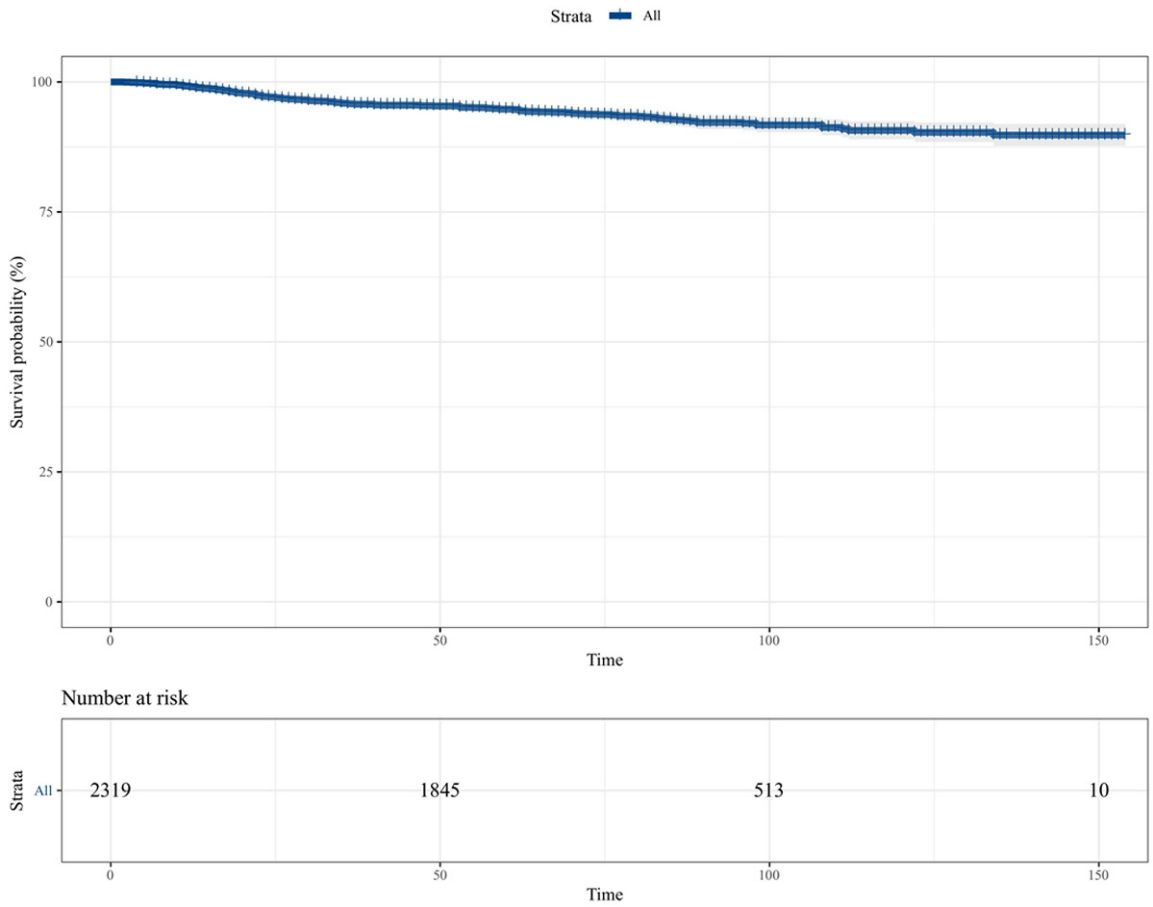

Figure S1. Kaplan-Meier curves demonstrating OS by survival in months based on all patients.