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Prognostic nomograms for locally advanced cervical cancer based on the SEER database

Integrating Cox regression and competing risk analysis

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Abstract

Locally advanced cervical carcinoma (LACC) remains a significant global health challenge owing to its high recurrence rates and poor outcomes, despite current treatments. This study aimed to develop a comprehensive risk stratification model for LACC by integrating Cox regression and competing risk analyses. This was done to improve clinical decision making. We analyzed data from 3428 patients with LACC registered in the Surveillance, Epidemiology, and End Results program and diagnosed them between 2010 and 2015. Cox regression and competing risk analyses were used to identify the prognostic factors. We constructed and validated nomograms for overall survival (OS) and disease-specific survival (DSS). Multivariate Cox regression identified key prognostic factors for OS, including advanced International Federation of Gynecology and Obstetrics stage, age, marital status, ethnicity, and tumor size. Notably, International Federation of Gynecology and Obstetrics stages IIIA, IIIB, and IVA had hazard ratios of 2.227, 2.451, and 4.852, respectively, significantly increasing the mortality risk compared to stage IB2. Ethnic disparities were evident, with African Americans facing a 39.8% higher risk than Caucasians did. Competing risk analyses confirmed the significance of these factors in DSS, particularly tumor size. Our nomogram demonstrated high predictive accuracy, with area under the curve values ranging from 0.706 to 0.784 for DSS and 0.717 to 0.781 for OS. Calibration plots and decision curve analyses further validated the clinical utility of this nomogram. We present effective nomograms for LACC risk stratification that incorporate multiple prognostic factors. These models provide a refined approach for individualized patient management and have the potential to significantly enhance therapeutic strategies for LACC.

Abbreviations: AC = adenocarcinoma, ACA = Affordable Care Act, AJCC7 = 7th edition of the American Joint Committee on Cancer (AJCC7), APC = annual percentage changes, AUC = area under the curve, CCRT = concurrent chemoradiotherapy, DCA = decision curve analysis, DSS = disease-specific survival, FIGO = International Federation of Gynecology and Obstetrics, HR = hazard ratio, LACC = locally advanced cervical carcinoma, OS = overall survival, ROC = receiver operating characteristic, SEER = Surveillance, Epidemiology, and End Results.

Keywords: competing risk analysis, Cox regression, locally advanced cervical carcinoma, nomogram, prognostic factors, SEER registry

1. Introduction

According to the 2020 Global Cancer Observatory statistics, cervical carcinoma remains a significant global health challenge with approximately 604,127 new cases and 341,831 deaths worldwide.[1] Locally advanced cervical carcinoma (LACC), classified as International Federation of Gynecology and Obstetrics (FIGO) stage IB-IVA, remains a critical concern.[2–5] Despite advancements in early detection and prevention, many patients are still being diagnosed with LACC.

Concurrent chemoradiotherapy (CCRT) is the standard treatment for LACC; CCRT, it often results in suboptimal outcomes, including high recurrence rates and severe side effects.[3–7] The complexity of treatment is further compounded by prognostic factors such as age, ethnicity, marital status, tumor size, FIGO staging, and histopathological evaluations.[8–11] Therefore, effective management of LACC is a multifaceted challenge.

Our study adopted a dual approach, employing Cox regression and competing risk analyses. Cox regression was chosen for its flexibility and effectiveness in identifying key survival factors in LACC. Competing risk analyses offer insights into the clinical outcomes.[12–18]

YZ and Y-PM contributed equally to this work.

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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Our goal was to integrate these methodologies to create a comprehensive and nuanced risk stratification model that significantly enhances clinical decision making in LACC. Utilizing data from the Surveillance, Epidemiology, and End Results (SEER) registry, we aimed to identify independent prognostic factors and validate our predictive models, addressing the pressing need for more effective LACC treatment strategies.

2. Materials and methods

2.1. Ethical review

Our analysis utilized data released from an online publicly available SEER database. This study was exempt from local research ethics committee approval, considering that SEER data were de-identified and publicly available for research use.

2.2. Datasets and patients

We analyzed the incidence and outcomes of LACC from 2010 to 2015 using data from the SEER Research Plus Data 18 registry. We adhered to the 7th edition of the American Joint Committee on Cancer (AJCC7) Cancer Staging System, focusing on patients age ≥18 years who met FIGO 2009 guidelines, with confirmed diagnoses of either squamous cell carcinoma or adenocarcinoma (AC) as their primary malignancy.[19–22] Patients with distant metastases or those with incomplete data were excluded from the study. The study period was selected based on the available and specific variables. Ethical approval was not required owing to the de-identified nature of the SEER database, and the Helsinki Declaration guidelines were followed.

Patient demographics included race, age, marital status, histological grade, TNM stage, pathological subtypes, treatment modalities, survival time, vital status, and the cause of death. TNM staging was reassessed per FIGO 2009 standards, and AJCC7 cervical cancer grading guidelines were strictly followed. Treatment options included radiation monotherapy, combined chemoradiotherapy, and surgery, with the main radiation methods being external beam radiation, brachytherapy, or both. Patients with 0 or unknown survival times were excluded.

2.3. Outcomes

The primary outcome was overall survival (OS), defined as the time from LACC diagnosis to death from any cause. The secondary outcome was disease-specific survival (DSS), defined as the period from diagnosis to death due to LACC. Deaths from other causes were considered competing risk factors.

2.4. Incident analysis of LACC from 2010 to 2015

The incidence rate, adjusted for age using the 2000 US Standard Population, was calculated as the number of cases per million annually between 2010 and 2015.[23,24] The annual percentage changes (APC) were determined using weighted least squares analysis.

2.5. Nomogram construction and validation

The SEER dataset of 3428 patients was divided into a training cohort (n = 2399) and validation cohort (n = 1029) in a 7:3 ratio. Prognostic and competing risk analyses were conducted in the training cohort and were validated in the validation cohort.

2.6. Cox regression analysis and nomogram for OS

We used both univariate and multivariate Cox regression analyses to identify independent prognostic factors, focusing on those with *P*-values <0.05 in univariate analysis. We then developed nomograms to predict 1-, 3-, 5-, and 7-year survival risks by assigning unique points to each variable. X-tile software (version 3.6.1) was used to classify the patients into low-, medium-, or high-risk categories.[25,26]

2.7. Competing risk analysis and nomogram for DSS

Competing risks were evaluated using the cumulative incidence function and Fine-Gray competing risk regression, employing the "cmprsk" R package.[27] We focused on deaths directly caused by LACC.

2.8. Nomogram validation for OS and DSS

Model predictions were evaluated using calibration curves and decision curve analysis (DCA) in both cohorts. Receiver operating characteristic (ROC) curve analysis was used to assess the predictive accuracy.

2.9. Online predictive tools for OS and DSS

Digital tools for OS and DSS assessments in LACC patients were developed using the "DynNom" and "Shiny" R packages and the Shiny website (https://www.shinyapps.io/).

2.10. Statistical analysis

Baseline categorical variables were presented as frequencies and percentages, and continuous variables were presented as mean ± standard deviation or interquartile range. The "surv_cutpoint" function in R (version 4.3.1)'s "survminer" package was applied to determine optimal cutoffs for age and tumor size. Categorical data comparisons were performed using Pearson chi-square test or Fisher exact test. Kaplan–Meier survival estimation and log-rank tests were used to assess OS and DSS. Cox regression and competing risk analyses were used to evaluate risk factors, with statistical significance set at $P < .05$.

3. Results

3.1. Incident and patient baseline characteristics

From 2010 to 2015, the incidence of LACC displayed a U-shaped trend (Fig. 1), initially decreasing and then increasing, with a significant APC ($P < .05$). Among the 3428 participants, the majority were White (73.0%), followed by Black (14.6%), and other races (12.3%), with no significant racial differences between the training and validation groups ($P = .263$). The median age was 49 years (IQR: 40–60), with similar age distributions in both the groups ($P = .326$). Surgery was not performed in 59.8% of patients, which was consistent across both groups ($P = .849$). Treatment modalities varied but showed no significant group differences ($P > .2$). The median tumor size was 51 mm (IQR: 40–68 mm), and the survival outcomes were comparable between the groups ($P > .1$). Detailed demographics are presented in Table 1.

3.2. Cutoff values for age and tumor size

Age and tumor size cutoff values were established at 64 mm and 58 mm, respectively (Fig. 2). Kaplan–Meier curves using these thresholds showed significant differences ($P < .0001$).

3.3. Cox regression analysis for OS

The multivariate analysis identified several significant prognostic factors. Age, advanced FIGO stage, histological grade, marital status, ethnicity, and treatment modality significantly

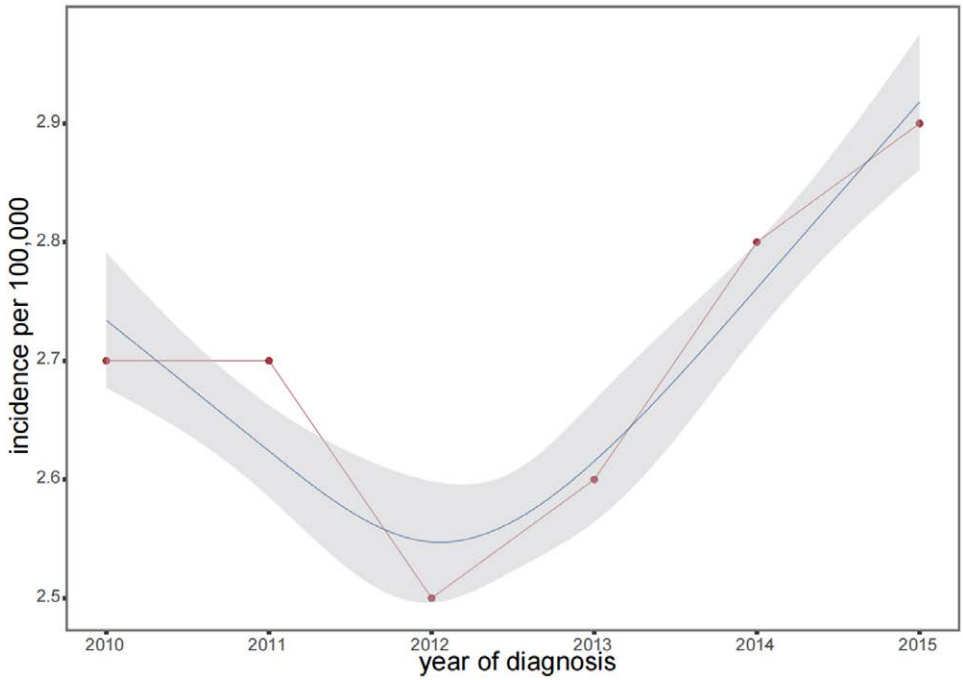

Figure 1. Trends in the annual age-adjusted incidence of LACC from 2010 to 2015. The vertical axis represents the number of cases per 100,000 individuals, while the horizontal axis shows the year of diagnosis. Data points are marked in red, depicting a "U-shaped" pattern over the 6-year timeframe. The incidence rate per 100,000 was 0.27 in 2010, dropped to 0.25 in 2012, and then steadily increased to 0.29 by 2015. The gray area in the graph indicates the confidence interval for the incidence rates, providing a visual representation of the range of data fluctuations. LACC = locally advanced cervical cancer.

influenced survival risks (Table 2). Notably, advanced stages and poor histological grades contributed to the risk, whereas treatment modes such as beam radiation and brachytherapy reduced this risk. Each unit increase in tumor size also increased risk (hazard ratio (HR) = 1.004, $P < .001$).

3.4. Competing risk analysis for DSS

Similar patterns were observed in DSS analysis, with advanced FIGO stages and racial disparities significantly impacting the risk. Radiation treatment notably reduced the risk, and tumor size remained an independent prognostic factor (Table 3).

3.5. Developing nomograms and risk stratification

Using the training cohort, we developed nomograms to predict OS and DSS in patients with LACC. We stratified the patients into low-, intermediate-, and high-risk groups, each demonstrating distinct survival trajectories over 7 years (see Figs. 3 and 4). Significant variations in survival rates were observed among the risk categories. Table 4 details the median survival times alongside the critical 1-, 3-, 5-, and 7-year survival probabilities segmented by risk group.

3.6. Validation of OS and DSS nomograms

Multiple validation methods confirmed the reliability and performance of the nomograms. Figure S1, Supplemental Digital Content, http://links.lww.com/MD/N864 and Figure S2, Supplemental Digital Content, http://links.lww.com/MD/N864 depict the OS and DSS ROC curves, respectively, for both the training and validation cohorts, over 1 to 7 years. The ROC curves demonstrated high accuracy, with area under the curve (AUC) values ranging from 0.717 to 0.781 for OS and 0.706 to 0.784 for DSS, underscoring the precision of the nomograms. The calibration plots for these survival metrics are presented in Figure S3, Supplemental Digital Content, http://links.lww.com/MD/N864 and Figure S4, Supplemental Digital Content, http://links.lww.com/MD/N864 which further reinforce the predictive validity of the models. DCA across various time points substantiated the substantial clinical benefits of nomograms within a wide range of threshold probabilities (Figure S5, Supplemental Digital Content, http://links.lww.com/MD/N864 and Figure S6, Supplemental Digital Content, http://links.lww.com/MD/N864). In addition, we developed 2 online tools for efficient and user-friendly survival prediction for OS (https://zhangying123.shinyapps.io/DynNomapp_cox/) and DSS (https://zhangying123.shinyapps.io/DynNomapp_CRM/).

4. Discussion

Cervical cancer poses a significant global health challenge, with 604,127 new cases and 341,831 deaths annually.[1] Patients with LACC face even greater treatment complexity. Despite advancements in early screening and preventive measures, current treatment options, such as CCRT, exhibit limited efficacy owing to their high recurrence rates and severe adverse effects.[3–7] Moreover, prognostic factors, such as age, race, marital status, and tumor size, further complicate treatment strategies.[8–11] In our study, we used data from the SEER database and employed Cox regression and competing risk analyses to address these intricacies. Our objective was to establish a comprehensive risk stratification model to guide precise clinical interventions.

Our study revealed a distinctive pattern in LACC prevalence between 2010 and 2015. Utilizing data from the SEER database, we observed an initial decrease from 0.27 per million in 2010 to 0.25 per million in 2012. This was followed by an increase to 0.29 per million followed this. This trend was statistically significant, with APC significantly different from zero ($P < .05$). Notably, this period coincided with the Affordable Care Act enactment in 2010. The initial decline in LACC prevalence could potentially be attributed to Affordable Care Act's enhancement of access to preventive healthcare services, such as

Table 1

Baseline demographic and clinical characteristics of patients with LACC.

	level	Overall	Training	Validation	*P*
n		3428	2399	1029	
Race (%)	White	2504 (73.046)	1733 (72.238)	771 (74.927)	.263
	Black	501 (14.615)	360 (15.006)	141 (13.703)	
	Other	423 (12.340)	306 (12.755)	117 (11.370)	
Age (median [IQR])		49.000 [40.000, 60.000]	49.000 [40.000, 60.000]	48.000 [39.000, 59.000]	.326
Marital status (%)	Married	1414 (41.249)	980 (40.850)	434 (42.177)	.493
	Single	2014 (58.751)	1419 (59.150)	595 (57.823)	
Histology (%)	SCC	2782 (81.155)	1942 (80.950)	840 (81.633)	.674
	AC	646 (18.845)	457 (19.050)	189 (18.367)	
Grade (%)	I	236 (6.884)	178 (7.420)	58 (5.637)	.238
	II	1546 (45.099)	1082 (45.102)	464 (45.092)	
	III	1573 (45.887)	1086 (45.269)	487 (47.328)	
	IV	73 (2.130)	53 (2.209)	20 (1.944)	
FIGO (%)	IB2	505 (14.732)	337 (14.048)	168 (16.327)	.516
	IIA1	120 (3.501)	83 (3.460)	37 (3.596)	
	IIA2	188 (5.484)	138 (5.752)	50 (4.859)	
	IIB	671 (19.574)	477 (19.883)	194 (18.853)	
	IIIA	67 (1.954)	51 (2.126)	16 (1.555)	
	IIIB	1743 (50.846)	1219 (50.813)	524 (50.923)	
	IVA	134 (3.909)	94 (3.918)	40 (3.887)	
Sequence (%)	No surgery	2051 (59.831)	1446 (60.275)	605 (58.795)	.849
	RAS	1224 (35.706)	847 (35.306)	377 (36.638)	
	RPTS	131 (3.821)	90 (3.752)	41 (3.984)	
	RBAS	22 (0.642)	16 (0.667)	6 (0.583)	
Surgery (%)	Not recommended	1894 (55.251)	1326 (55.273)	568 (55.199)	.222
	SP	1486 (43.349)	1034 (43.101)	452 (43.926)	
	RBNP	48 (1.400)	39 (1.626)	9 (0.875)	
Radiation (%)	None	338 (9.860)	236 (9.837)	102 (9.913)	.961
	Beam radiation	1375 (40.111)	964 (40.183)	411 (39.942)	
	brachytherapy	268 (7.818)	191 (7.962)	77 (7.483)	
	CBB	1447 (42.211)	1008 (42.018)	439 (42.663)	
Chemotherapy (%)	No	604 (17.620)	430 (17.924)	174 (16.910)	.506
	Yes	2824 (82.380)	1969 (82.076)	855 (83.090)	
Tumor size (median [IQR])		51.000 [40.000, 68.000]	50.000 [40.000, 68.000]	55.000 [40.000, 70.000]	.127
Cause of death (%)	Alive	2110 (61.552)	1457 (60.734)	653 (63.460)	.173
	Cervix Uteri	992 (28.938)	701 (29.221)	291 (28.280)	
	other	326 (9.510)	241 (10.046)	85 (8.260)	
Time (median [IQR])		45.500 [21.000, 69.000]	46.000 [21.000, 69.000]	45.000 [21.000, 71.000]	.822
Death (%)	Alive	2110 (61.552)	1457 (60.734)	653 (63.460)	.143
	Dead	1318 (38.448)	942 (39.266)	376 (36.540)	

AC = adenocarcinoma; CI = confidence interval; CBB = combined beam with brachytherapy; FIGO = International Federation of Gynecology and Obstetrics; Grade I = well-differentiated; Grade II = moderately differentiated; Grade III = poorly differentiated; Grade IV = undifferentiated; HR = hazard ratio; LACC = locally advanced cervical carcinoma; *P* = *P*-value; RAS = radiation after surgery; RBAS = radiation before and after surgery; RBNP = recommended but not performed; RPTS = radiation prior to surgery; SCC = squamous cell carcinoma; SP = surgery performed.

cervical cancer screenings. However, the increase in prevalence from 2012 to 2015 suggests that other factors, such as rising healthcare costs, coverage gaps, or social determinants affecting risk, may have contributed to this observed trend.[28–32]

Our investigation pioneered the LACC prognosis by establishing apparent age and tumor size thresholds of 64 and 58 mm, respectively. This significantly affects patient outcomes. Through Kaplan–Meier analyses, we demonstrated the statistical significance of the survival outcomes associated with these thresholds ($P < .0001$), highlighting their clinical relevance. Unlike previous studies that predominantly relied on vague mean or median age ranges, our study innovatively defined a clinically operational age cutoff based on survival metrics.[33–36] This addition fills the existing knowledge gaps and has the potential to revolutionize personalized treatment, particularly for geriatric populations. Equally significant is the establishment of a 58 mm threshold for tumor size, serving as a measurable benchmark for therapeutic and prognostic assessments. Tumors exceeding this threshold indicate a more aggressive disease phenotype and necessitate tailored and intensive treatment. Prior studies offer descriptive measures, making our Kaplan–Meier-supported threshold a valuable clinical tool.[37–39]

Our analyses also revealed a multifaceted landscape of risk factors, including advanced FIGO stage, histological grade, and racial disparities. These factors significantly affected OS and DSS. Our study's emphasis on the significance of advanced FIGO stages and age closely aligns with a recent multicenter study that focused on LACC. That study found that AC/adenosquamous histology was associated with a lower pathological complete response and a higher risk of recurrence and death than squamous cell carcinoma. This suggests that histological type may also play a crucial role in patient outcomes.[40] Significant racial disparities existed, with Black patients facing an increased risk of DSS disparities (HR = 1.334, $P = .006$). This aligns with findings from previous studies, which indicated that Black women with advanced cervical cancer are less likely to receive brachytherapy. This results in differences in survival rates among racial groups.[41] Therefore, it is imperative to adopt a comprehensive and equitable approach to patient care. Effective treatment modalities such as radiation therapy and brachytherapy, along with surgical interventions, significantly reduced the risk of both OS (HR = 0.528, $P < .001$) and DSS (HR = 0.641, both $P < .02$), as previously demonstrated.[42–46] These findings confirm the effectiveness of these treatments and suggest their applicability in a broader

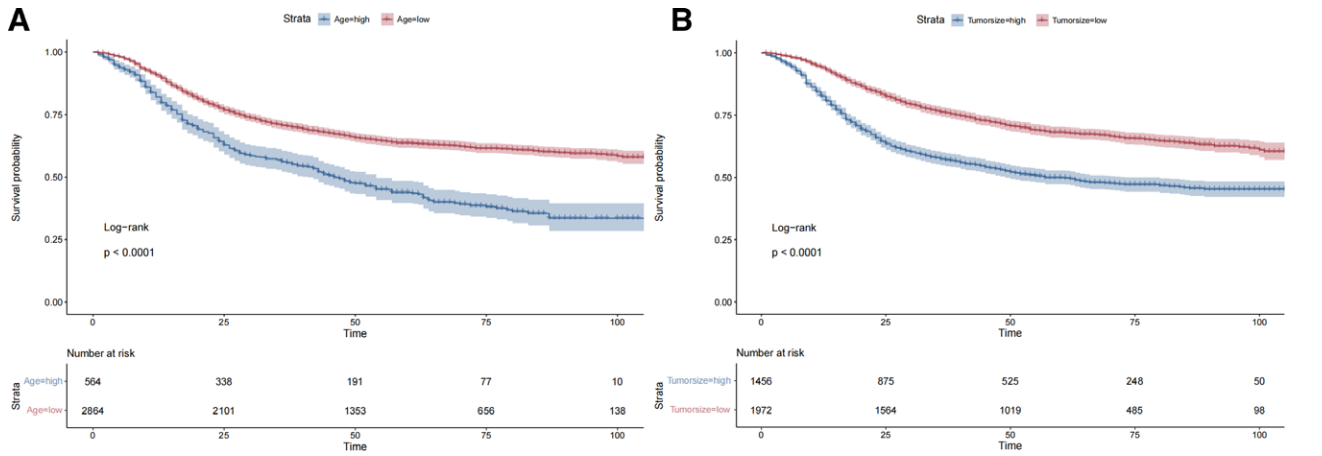

Figure 2. Optimal cutoff values for age and tumor size in LACC patients. (A) The survival curve for age and (B) for tumor size. Both curves demonstrate statistically significant differences, with *P*-values <.0001. Survival probability decreases over time, with lower survival rates observed in the older age group and the larger tumor size group. The "Strata" labels indicate different risk groups, with blue representing the low-risk group (younger age/smaller tumor) and red indicating the high-risk group (older age/larger tumor). The table below each point in time displays the number of patients at risk at that time. LACC = locally advanced cervical carcinoma.

Table 2

Univariate and multivariate Cox proportional hazards analyses of factors affecting OS in LACC patients.

	Univariate analysis		Multivariate analysis	
Variable	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***
Age	1.017 (1.012–1.021)	<0.001	1.015 (1.01–1.019)	<.001
Chemotherapy				
Yes vs no	0.867 (0.737–1.02)	0.085	NA	NA
FIGO				
IIA1 vs IB2	1.186 (0.748–1.883)	0.468	1.35 (0.843–2.161)	.211
IIA2 vs IB2	1.456 (1.015–2.087)	0.041	1.432 (0.994–2.063)	.054
IIB vs IB2	1.297 (0.991–1.698)	0.058	1.36 (1.025–1.804)	.033
IIIA vs IB2	2.592 (1.657–4.054)	<0.001	2.173 (1.378–3.425)	.001
IIIB vs IB2	2.099 (1.666–2.644)	<0.001	2.475 (1.941–3.155)	<.001
IVA vs IB2	5.395 (3.923–7.421)	<0.001	4.552 (3.276–6.325)	<.001
Grade				
II vs I	1.245 (0.939–1.651)	0.128	1.166 (0.875–1.555)	.295
III vs I	1.523 (1.152–2.014)	0.003	1.4 (1.053–1.863)	.021
IV vs I	2.126 (1.362–3.317)	0.001	2.087 (1.332–3.27)	.001
Histology				
AC vs SCC	0.82 (0.693–0.97)	0.02	1.014 (0.849–1.212)	.874
Marital status				
Single vs married	1.257 (1.101–1.434)	0.001	1.175 (1.026–1.346)	.02
Race				
Black vs White	1.499 (1.272–1.766)	<0.001	1.398 (1.179–1.657)	<.001
Other vs White	0.956 (0.78–1.172)	0.666	0.972 (0.791–1.194)	.786
Radiation				
Beam radiation vs none	0.799 (0.649–0.984)	0.035	0.554 (0.421–0.728)	<.001
Brachytherapy vs none	0.694 (0.517–0.933)	0.015	0.433 (0.306–0.611)	<.001
CBB vs none	0.606 (0.491–0.749)	<0.001	0.392 (0.297–0.519)	<.001
Sequence				
RAS vs no surgery	0.504 (0.434–0.584)	<0.001	0.953 (0.74–1.228)	.711
RPTS vs no surgery	0.699 (0.49–0.997)	0.048	1.605 (1.053–2.448)	.028
RBAS vs no surgery	1.549 (0.853–2.811)	0.15	3.093 (1.623–5.894)	.001
Surgery				
SP vs not recommended	0.542 (0.473–0.621)	<0.001	0.528 (0.41–0.679)	<.001
RBNP vs not recommended	0.946 (0.592–1.512)	0.817	0.808 (0.504–1.296)	.377
Tumor size	1.004 (1.003–1.005)	<0.001	1.004 (1.003–1.005)	<.001

AC = adenocarcinoma; CI = confidence interval; CBB = combined beam with brachytherapy; HR = hazard ratio; RAS = radiation after surgery; LACC = locally advanced cervical carcinoma; OS = overall survival; RBAS = radiation before and after surgery; RBNP = recommended but not performed; RPTS = radiation prior to surgery; SCC = squamous cell carcinoma; SP = surgery performed.

range of patients. These results underscore the importance of early intervention and advocate for a more holistic approach to patient care.

Our study introduced robust nomograms that accurately predicted OS and DSS in patients with LACC. These models underwent rigorous validation and demonstrated high discriminative capabilities, with AUCs ranging from 0.717 to 0.781 for OS and 0.706 to 0.784 for DSS.[47] The calibration curves and DCA support the reliability and clinical utility of these nomograms. Our risk stratification method categorized patients into

Table 3

Univariate and multivariate competing risks analyses of DSS in patients with LACC.

	Univariate analysis		Multivariate analysis	
Variable	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***
Age	1.001 (0.996–1.007)	.690	–	–
Chemotherapy				
Yes vs no	1.01 (0.829–1.232)	.920	–	–
FIGO				
IIA1 vs IB2	1.071 (0.613–1.869)	.810	1.32 (0.742–2.349)	.340
IIA2 vs IB2	1.442 (0.943–2.206)	.091	1.457 (0.941–2.258)	.092
IIB vs IB2	1.188 (0.86–1.642)	.300	1.252 (0.884–1.772)	.210
IIIA vs IB2	2.484 (1.445–4.27)	.001	2.227 (1.245–3.984)	.007
IIIB vs IB2	2.226 (1.694–2.925)	<.001	2.451 (1.829–3.283)	<.001
IVA vs IB2	5.382 (3.669–7.895)	<.001	4.852 (3.256–7.23)	<.001
Grade				
II vs I	1.092 (0.799–1.491)	.580	1.019 (0.729–1.424)	.910
III vs I	1.374 (1.01–1.87)	.043	1.261 (0.905–1.758)	.170
IV vs I	1.793 (1.1–2.923)	.019	1.705 (1.039–2.798)	.035
Histology				
AC vs SCC	0.768 (0.632–0.934)	.008	0.931 (0.75–1.157)	.520
Marital status				
Single vs married	1.204 (1.035–1.401)	.016	1.131 (0.964–1.326)	.130
Race				
Black vs White	1.429 (1.18–1.729)	<.001	1.334 (1.087–1.638)	.006
Other vs White	0.932 (0.736–1.182)	.560	1.027 (0.806–1.308)	.830
Radiation				
Beam radiation vs none	0.89 (0.692–1.144)	.360	0.641 (0.457–0.898)	.010
Brachytherapy vs none	0.876 (0.625–1.228)	.440	0.613 (0.407–0.922)	.019
CBB vs none	0.711 (0.552–0.915)	.008	0.493 (0.35–0.694)	<.001
Sequence				
RAS vs no surgery	0.543 (0.459–0.642)	<.001	0.959 (0.725–1.269)	.770
RPTS vs no surgery	0.662 (0.433–1.013)	.058	1.343 (0.838–2.153)	.220
RBAS vs no surgery	2.216 (1.352–3.632)	.002	3.843 (2.15–6.868)	<.001
Surgery				
SP vs not recommended	0.549 (0.469–0.642)	<.001	0.555 (0.417–0.738)	<.001
RBNP vs not recommended	1.071 (0.654–1.753)	.790	0.92 (0.545–1.552)	.750
Tumor size	1.004 (1.002–1.006)	<.001	1.004 (1.003–1.005)	<.001

AC = adenocarcinoma; CI = confidence interval; CBB = combined beam with brachytherapy; DSS = disease-specific survival; HR = hazard ratio; LACC = locally advanced cervical carcinoma; RAS = radiation after surgery; RBAS = radiation before and after surgery; RBNP = recommended but not performed; RPTS = radiation prior to surgery; SCC = squamous cell carcinoma; SP = surgery performed.

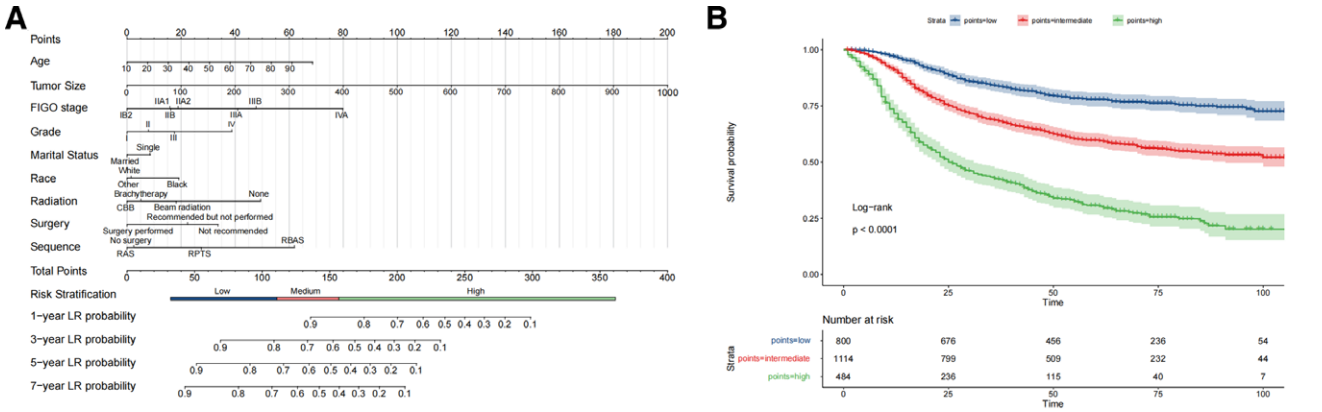

Figure 3. Prognostic evaluation of OS in LACC using nomograms and risk stratification. (A) A detailed nomogram that estimates the probability of 1-, 3-, 5-, and 7-year OS based on a range of clinical and demographic variables. Points are assigned to age, tumor size, FIGO stage, histological grade, marital status, race, type of radiation therapy, surgical intervention, and sequence of treatment. This results in a total score that corresponds to a risk stratification category and survival probability. (B) Kaplan–Meier survival curves stratified into high, intermediate, and low-risk groups based on the total points calculated from the nomogram. The curves provide a visual representation of survival probabilities over time for each risk group. A log-rank test confirms the statistical significance of differences observed. The number of patients at risk at various time points is also indicated, providing context for the survival probabilities displayed. The low-risk group shows high survival resilience, with a 1-year survival rate of 96.9% and a 7-year rate of 75.0%. Intermediate-risk patients have a 1-year survival rate of 91.0%, which decreases to 54.5% at 7 years. The high-risk group starts at a 1-year survival rate of 71.6%, dropping dramatically to 24.8% at 7 years, demonstrating the most significant decline. OS = overall survival; FIGO = International Federation of Gynecology and Obstetrics; LACC = locally advanced cervical carcinoma.

low-, intermediate-, and high-risk cohorts, revealing distinct temporal survival patterns over 1-, 3-, 5-, and 7-year intervals, respectively. The low-risk group demonstrated a resilient survival trend, with a survival rate of 75.0% over year 7. Simultaneously, the high-risk cohort experienced a significant decline, with a survival rate of only 24.8% at the same interval. Similar patterns were observed in DSS outcomes, underscoring the importance of personalized risk-adapted strategies

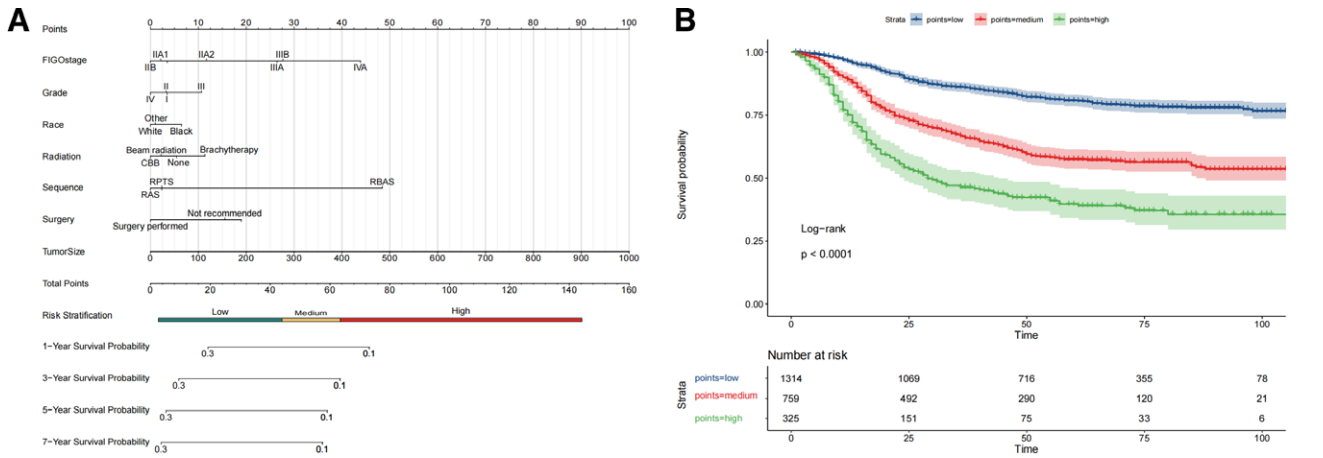

Figure 4. Prognostic nomogram and survival curves for DSS in LACC. (A) A nomogram that assigns points to clinical variables such as FIGO stage, histological grade, race, type of radiation therapy, surgery sequence, and tumor size. This culminates in a total score that indicates a patient's risk category and corresponding survival probabilities at 1, 3, 5, and 7 years. (B) Kaplan–Meier survival curves segmented into high, medium, and low-risk groups as determined by the nomogram's scoring system. These curves visually represent the differences in survival rates over time among the risk categories, with statistical validation provided by the log-rank test. The number at risk at various time intervals is also noted, offering a detailed view of survival trends according to stratified risk groups. The low-risk cohort maintains excellent survival rates, starting at 96.5% at 1 year and declining to 78.0% at 7 years. The intermediate-risk cohort experienced a more pronounced decrease from 89.0% at 1 year to 56.4% at 7 years. The high-risk category showed the steepest decline, from 75.1% at 1 year to 35.6% at 7 years, highlighting the severity of risk associated with this group. DSS = disease-specific survival; FIGO = International Federation of Gynecology and Obstetrics; LACC = locally advanced cervical carcinoma.

Table 4

Survival rates by risk stratification for OS and DSS in LACC (in months).

Risk group		Median time	1-year rate	3-year rate	5-year rate	7-year rate
OS	High risk	26 (23–31)	71.6 (67.6–75.7)	42.5 (38.2–47.2)	20.7 (26.5–35.5)	24.8 (20.4–30.0)
	Medium risk	Not reached (95% CI NA–NA)	91.0 (89.3–92.7)	68.7 (66.0–71.5)	59.7 (56.8–62.9)	54.5 (51.1–58.1)
	Low risk	Not reached (95% CI NA–NA)	96.9 (95.7–98.1)	84.0 (81.4–86.6)	77.8 (74.7–80.9)	75.0 (71.5–78.5)
DSS	High risk	29 (24–44)	75.1 (70.4–80.0)	46.3 (40.9–52.4)	39.7 (34.2–46.2)	35.6 (29.6–43.0)
	Medium risk	Not reached (95% CI NA–NA)	89.0 (86.8–91.3)	66.7 (63.3–70.3)	57.4 (53.7–61.5)	56.4 (52.5–60.5)
	Low risk	Not reached (95% CI NA–NA)	96.5 (95.4–97.5)	86.1 (84.2–88.1)	80.8 (78.5–83.2)	78.0 (75.4–80.7)

CI = confidence interval; DSS = disease-specific survival; LACC = locally advanced cervical carcinoma; NA = unavailable; OS = overall survival.

for managing LACC. The effectiveness of our nomogram was further enhanced by incorporating multiple independent prognostic factors, including the FIGO stage, age, histological grade, and treatment modality. This contributed to the predictive accuracy of the model. A multidimensional approach is essential for optimizing patient outcomes. We implemented these nomograms, accessible through user-friendly online tools for both OS and DSS, providing clinicians with a convenient interface for individual patient risk assessment and survival prediction.

This study has some limitations. First, the SEER dataset we utilized lacked essential biomarkers, including HPV DNA, P16INK4A, and Ki-67, which are critical for prognostic assessment.[48–54] Additionally, the database lacks complete treatment details, such as surgical techniques, chemotherapy regimens, radiotherapy doses, tumor morphology, comorbidities, and socioeconomic factors that influence survival.[55,56] The absence of imaging data limits the ability of deep learning approaches to enhance model accuracy. Owing to these unaccounted variables in our analysis, future studies should consider incorporating these key factors to improve their clinical relevance.

5. Conclusions

By analyzing data from the SEER database, our study delves into the intricate landscape of risk factors affecting OS and DSS rates among patients with LACC, yielding valuable insights. Our study introduces robust nomograms that have undergone rigorous validation, demonstrating a high predictive accuracy for survival outcomes. These nomograms pave the way for personalized risk-adapted treatment strategies. Our findings demonstrated the pivotal role of age, FIGO stage, histological grade, and racial disparity in predicting LACC prognosis. Importantly, our research established clinical, operational age, and tumor size cutoff values. This addresses a significant gap in the literature and provides a more nuanced approach to patient care.

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