A Novel Nomogram for Predicting Cancer-Specific Survival in Women with Uterine Sarcoma: A Large Population-Based Study

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Research

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Abstract

Background: To develop a comprehensive nomogram for predicting the cancer-specific survival (CSS) for uterine sarcoma (US).

Methods: 3861 patients of US between 2010 to 2015 were identified for this study from the Surveillance, Epidemiology, and End Results (SEER) database. They were randomly divided into a training cohort (n = 2702) and a validation cohort (n = 1159) in a 7-to-3 ratio by R software. Multivariate Cox regression analysis was performed to select predictive variables and then to identify independent prognostic factors. The concordance index (C-index), the area under the time-dependent receiver operating characteristics curve (AUC), the net reclassification improvement (NRI), the integrated discrimination improvement (IDI), calibration plotting, and decision-curve analysis (DCA) were used to compare the new survival nomogram with the AJCC 7th edition prognosis model.

Results: We have established a nomogram for determining the 1-, 3-, and 5-year CSS probabilities of US patients. In this nomogram, pathology grade has the highest risk on CSS in US, followed by the age at diagnosis, then surgery status. The C-index for the nomogram (0.796, 0.767 for the training and validation cohort, respectively) was higher than those for the AJCC staging system (0.706 and 0.713, respectively). Furthermore, AUC value, NRI, IDI, calibration plotting, and DCA showed that this nomogram exhibited better performance than the AJCC staging system alone.

Conclusion: Our study validated the first comprehensive nomogram for US which could provide more accurately and individualized survival predictions for US patients in clinical practice.

Background

Uterine Sarcoma (US) is a rare malignant uterine tumor in women that account for 3–7% of all uterine cancer cases [1] and is characterized by aggressive behavior and rapid progression. The incidence of US ranges from 1.55 to 1.95 per 100000 females per year [2]. Current classification of US includes endometrial stromal sarcoma, leiomyosarcoma, mixed epithelial and mesenchymal tumors according to the common histological types [3]. No common etiology has been identified, but several agents might be associated US, such as tamoxifen treatment, pelvic radiation therapy, and hereditary leiomyomatosis [4]. Management involves the coordination of multidisciplinary treatment including surgery, radiotherapy, chemotherapy and hormonal blockade. However, the 5-year survival rate is less than 50% in early stages and less than 15% in advanced stages [5,6].

The American Joint Committee on Cancer (AJCC) TNM staging system is the most extensively used clinical tool in determining the prediction of cancer [7], which is based on the extent of tumor (T), number of metastatic lymph nodes (N), and the presence of distant metastasis (M). However, US is a very heterogeneous disease. Patients' response to therapy differs widely and the survival rate varies at the same stage. It was known that some of the clinical characteristics such as age, race, tumor size were also noteworthy factors influencing individual survival outcomes of cancer patients [8,9]. For example, US is

twice more frequent among black women than that of white women, also, the risk of sarcoma is higher for women aged 50 years [10]. Thus, a novel exact prognostic tool which contains personalized characteristics is needed to improve the accuracy of prognosis in women with US.

Recently, nomogram which presented by grahphs is widely used to predict an outcome of malignant tumors. The purpose of this study was to develop a novel nomogram to predict the cancer-specific survival (CSS) of US patients based on a cohort from the SEER database, and to explore the relative demographic factors and clinicopathological features.

Methods

Data source

We searched and studied information on patients in the latest version of the SEER (covering 18 registries additional chemotherapy data), by using SEER*Stat version 8.3.6.1 (https://seer.cancer.gov/) [11–13]. US patients from the SEER database were extracted in certain ways. Firstly, we chose age at diagnosis, race, and marital status as demographic characteristics, then we selected the primary sites of US using the following codes “C54.0-Isthmus uteri”, “C54.1-Endometrium”, “C54.2-Myometrium”, “C54.3-Fundus uteri”, “C54.8-Overlapping lesion of corpus uteri”, “C54.9-Corpus uteri”, and “C55.9-Uterus, NOS”. According to the ICD-O-3 morphology codes, histological sub-types of US were defined as follows [10]:

- Sarcoma, NOS: “8800/3-8805/3”.
- Leiomyosarcoma: “8890/3: Leiomyosarcoma, NOS”, “8891/3: Epithelioid leiomyosarcoma”, “8896/3: myxoid leiomyosarcoma”.
- Adenosarcoma: “8933/3: Adenosarcoma”
- Stromal sarcoma: “8930/3: Endometrial stromal sarcoma”, “8931/3: Endometrial stromal sarcoma, low-grade”, “8935/3: Stromal sarcoma, NOS”.
- Carcinosarcoma: “8950/3: Mullerian mixed tumor”, “8951/3: Mesodermal mixed tumor”, “8980/3: Carcinosarcoma, NOS”.

We also chose the following pathological features in this study: SEER stage, pathology grade, tumor size, AJCC stage, surgery status, radiotherapy status, and chemotherapy status. We noticed that the summary stage in the SEER database has four levels: in situ, localized, regional, and distant. In our study, we only included the last three levels due to the lack of patient data in the first one. The tumor pathology grade is divided into the following four levels: Grade I (well differentiated), Grade II (moderately differentiated), Grade III (poorly differentiated), and Grade IV (undifferentiated or anaplastic). We used the AJCC stage based on the seventh edition of the Derived AJCC Stage Group. The tumor size was classified into three categories according to its diameter: ≤ 50, > 50 mm and unknown. We sorted the surgery status on the basis of the records in the SEER database. “Yes” means surgery performed, while “No” means no surgery performed due to three situations as follow: not recommended, patient died prior to recommended surgery, and recommended but patient refused. The radiotherapy status was also classified. “Yes” means

radiation preformed including beam radiation, radiation, radioactive implants, and combination of beam with implants or isotopes, while “No” means none/unknown, refused, or recommended but unknown if administered. We also classified the chemotherapy status. “Yes” means chemotherapy performed. “No” means not performed or unknown. The outcome in this study was death due to US.

Criteria For Data Selection

We excluded cases that were not confirmed by microscopy or only in an autopsy. The retrospective study initially identified 3922 uterine sarcoma patients enrolled in the SEER database from 2010 to 2015 by applying the criteria mentioned above. However, 60 patients were not included in the final analysis due to unknown insurance status and one with no tumor found. Finally, we selected 3861 US patients, 70% (n = 2702) of which were randomly assigned into the training cohort for constructing the prognostic nomogram and 30% (n = 1159) of which into the validation cohort for evaluating the constructed nomogram. Data screening process was shown in Fig. 1.

Statistical analysis

Twelve pathological and clinical features of age at diagnosis, race, marital status, insurance record, tumor site, pathology grade, histological type, SEER stage, AJCC stage, surgery status, radiotherapy status, and chemotherapy status were applied to conduct the analyses. The age at diagnosis data were expressed as mean ± SD, while other categorical variables were represented as percentages. We used Cox regression to screen for correlation factors ($p = 0.1$). Then, a novel nomogram which predicted the 1-, 3-, and 5-year CSS probabilities of US was established.

The concordance index (C-index) and the area under the time-dependent receiver operating characteristics (ROC) curves (AUC) were applied to evaluate the differentiation ability of this new model. We compared the accuracy and comprehensiveness of these two models using the net reclassification improvement (NRI) and the integrated discrimination improvement (IDI) in order to determine the improvement obtained from the new predictive model[14]. The consistency of survival probabilities predicted by the nomogram with the actual situation was assessed by charting calibration plots. The clinical validity of the predictive model was tested via decision curve analyses (DCA) [15].

Statistical analyses were conducted by using SPSS Statistics software (version 24.0, SPSS, Chicago, IL, USA) and R software (version 3.6.0; http://www.Rproject.org). We used R software to divide the 3922 patients into a 7-to-3 ratio to the two study cohorts randomly, then performed log-rank test to ensure that there were no significant differences between these two cohorts. The p-values less than 0.05 were considered to be statistically significant.

Ethical Review

Data on cancer research from the SEER was supported and managed by the National Cancer Institute. Since the aggregate data derived from the SEER database has been de-identified, informed patient consent is not required.

Results

Patients’ characteristics

3861 US patients extracted from the SEER database were divided via the popular random split-sample method (with a split ratio of 7:3) into 2702 in the training cohort and 1159 in the validation cohort. The median age at diagnosis was 62 years (interquartile range, 53–69 years) in the training and 60 years (interquartile range, 51–69 years) in validation cohorts. The majority of the patients in the training and validation were white (69.2 and 71.2%), married (47.6 and 48.3%), and insured (95.4 and 96.3%). Among the tumor-related features, most of the tumors were at pathological Grade III and Grand IV and bigger than 50 mm in both cohorts. Nearly half of the patients were histologically diagnosed with carcinosarcoma. The distribution of different SEER stages was close to agreement with a little higher rate in localized group (37.4 and 42.5%). Nearly half of the patients were in AJCC stage I (41.0 and 45.1%) and only less than one tenth of the patients were in AJCC stage II (9.7 and 8.1%). Most of the patients received surgery (90.8 and 92.4%), with a few receiving radiotherapy and over half receiving chemotherapy in both cohorts.

The characteristics of the patients in these two cohorts were summarized in Table 1.

Table 1
Patient characteristics in the study

Variable	Training Cohort (n = 2702)	Validation Cohort (n = 1159)
Medium age at diagnosis, (25th -75th percentile)	62 (53–69)	60 (51–69)
Race n (%)		
White	1869 (69.2)	808 (71.2)
Black	591 (22.1)	243 (20.2)
Other	242 (8.6)	108 (8.6)
Marital status n (%)		
Married	1257 (47.6)	561 (48.3)
Single	586 (22.3)	261 (22.7)
SDW	736 (25.6)	293 (25.5)
Unknown	123 (4.6)	44 (3.5)
Insurance record n (%)		
Yes	2584 (95.4)	1117 (96.3)
No	118 (4.6)	42 (3.7)
Tumor size n (%)		
≤ 50 mm	710 (23.1)	313 (23.8)
> 50 mm	1596 (61.4)	677 (61.6)
Unknown	396 (15.6)	169 (14.6)
Pathological grade n (%)		
I	169 (6.4)	76 (6.0)
II	345 (12.0)	135 (11.4)
III	1193 (43.0)	527 (44.5)
IV	995 (38.7)	421 (38.2)
Histological type n (%)		
Sarcoma	76 (4.3)	20 (2.8)
Leiomyosarcoma	532 (28.3)	215 (26.6)

Variable	Training Cohort (n = 2702)	Validation Cohort (n = 1159)
Adenosarcoma	124 (4.4)	45 (3.8)
Stromal sarcoma	455 (14.1)	207 (15.5)
Carcinosarcoma	1515 (48.8)	672 (51.3)
SEER stage n (%)		
Localized	1116 (37.4)	537 (42.5)
Regional	825 (29.1)	321 (28.2)
Distant	761 (33.5)	301 (29.3)
AJCC stage n (%)		
I	1225 (41.0)	573 (45.1)
II	236 (9.7)	84 (8.1)
III	572(20.0)	222 (20.0)
IV	669 (29.3)	280 (26.9)
Surgery status n (%)		
Yes	2516 (90.8)	1090 (92.4)
No/Unknown	186 (9.2)	69 (7.6)
Radiotherapy status n (%)		
Yes	782 (26.3)	313 (24.6)
No/Unknown	1920 (73.7)	846 (75.4)
Chemotherapy status n (%)		
Yes	1420 (52.4)	598 (53.2)
No/Unknown	1282 (47.6)	561 (46.8)

Variable Screening And Multivariate Cox Regression Analysis Results

Following variables in the Cox regression were used: age at diagnosis, race, marital status, insurance record, years of diagnosis, tumors' primary site, tumor size, pathology grade, histological type, SEER stage, AJCC stage, surgery status, surgery site, radiotherapy status, and chemotherapy status. There was no difference shown in the prognosis for US in different years of diagnosis, primary site, and surgery site

using Cox stepwise regression analysis. Therefore, data on age at diagnosis, race, marital status, insurance record, tumor size, pathology grade, histological type, SEER stage, AJCC stage, surgery status, radiotherapy status, and chemotherapy status were incorporated into multivariate Cox regression analyses. The following significant prognostic risk factors were revealed by Cox regression analysis: age at diagnosis [hazard ratio (HR) = 1.0116, $p < 0.001$], being black (HR = 1.1698, $p < 0.05$), single (HR = 1.2181 vs. married, $p < 0.05$), SDW (HR = 1.2965 vs. married, $p < 0.001$), tumor size > 50 mm (HR = 1.4861 vs. ≤ 50 mm, $p < 0.001$), tumor size unknown (HR = 1.3345 vs. ≤ 50 mm, $p < 0.01$), pathology grade III (HR = 7.3773 vs. pathology grade I, $p < 0.001$), and pathology grade IV (HR = 7.0185 vs. pathology grade I, $p < 0.001$), regional (HR = 1.8809 vs. localized, $p < 0.001$), distant (HR = 2.5199 vs. localized, $p < 0.001$), AJCC stage III (HR = 1.7459 vs. AJCC stage I, $p < 0.001$), and AJCC stage IV (HR = 2.2275 vs. AJCC stage I, $p < 0.001$). Meanwhile, we found that leiomyosarcoma (HR = 0.6550 vs. sarcoma, $p < 0.01$), carcinosarcoma (HR = 0.6099 vs. sarcoma, $p < 0.01$), insurance (no insurance HR = 1.4851, $p < 0.01$), receiving surgery (no/unknown surgery HR = 2.7559, $p < 0.001$), adjuvant radiotherapy (no/unknown radiotherapy HR = 1.3267, $p < 0.001$), and adjuvant chemotherapy (no/unknown chemotherapy HR = 1.5355, $p < 0.001$) were protective factors for surviving US. The results also indicated that other race, other marital status, pathology grade II, adenosarcoma, stromal sarcoma and AJCC stage II were not significant risk factors ($P > 0.05$). The variables selected in the multivariate Cox regression analysis were presented Table 2.

Table 2
Selected variables in the SEER database by multivariate Cox regression analysis (training cohort)

Variable	Hazard ratio	95% CI	*p* value
Age at diagnosis	1.0116	1.0061–1.0172	0.000***
Race			
White	Reference		
Black	1.1698	1.0225–1.3383	0.022*
Other	0.8481	0.6698–1.0739	0.171
Marital status			
Married	Reference		
Single	1.2181	1.0436–1.4217	0.012*
SDW	1.2965	1.1230–1.4969	0.000***
Other	1.2816	0.9740–1.6863	0.076
Insurance record			
Yes	Reference		
No	1.4851	1.1367–1.9404	0.004**
Tumor size			
≤ 50 mm	Reference		
> 50 mm	1.4861	1.2674–1.7425	0.000***
Unknown	1.3345	1.0802–1.6487	0.007**
Pathological grade			
I	Reference		
II	1.3135	0.7662–2.2518	0.321
III	7.3773	4.5441–11.9771	0.000***
IV	7.0185	4.3528–11.3165	0.000***
Histological type			
Sarcoma	Reference		

SDW Separated, divorced, and widowed, *SEER* Surveillance, Epidemiology, and End Results, *HR* hazard ratio, *AJCC* American Joint Committee on cancer

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$

Variable	Hazard ratio	95% CI	*p* value
Leiomyosarcoma	0.6550	0.4839–0.8866	0.006**
Adenosarcoma	0.6288	0.3919–1.0089	0.054
Stromal sarcoma	0.9274	0.6623–1.2984	0.661
Carcinosarcoma	0.6099	0.4535–0.8202	0.001**
SEER stage			
Localized	Reference		
Regional	1.8809	1.3831–2.5580	0.000***
Distant	2.5199	1.6708–3.8005	0.000***
AJCC stage			
I	Reference		
II	1.0136	0.7096–1.4478	0.941
III	1.7459	1.2843–2.3735	0.000***
IV	2.2275	1.4818–3.3484	0.000***
Surgery status			
Yes	Reference		
No/Unknown	2.7559	2.2503–3.3751	0.000***
Radiotherapy status			
Yes	Reference		
No/Unknown	1.3267	1.1567–1.5216	0.000***
Chemotherapy status			
Yes	Reference		
No/Unknown	1.5355	1.3509–1.7453	0.000***

SDW Separated, divorced, and widowed, *SEER* Surveillance, Epidemiology, and End Results, *HR* hazard ratio, *AJCC* American Joint Committee on cancer

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$

Nomogram Construction

Figure 2 showed the nomogram for predicting the 1-, 3-, and 5-year CSS probabilities for US patients which was established based on the data for the multivariate Cox regression model in Table 1. The pathological grade was set as reference scale ranging from 0 to 100 because it had the largest coefficient absolute value. Then each predictor had its factors with points and marks on its line based on the set scale. The total points of the nomogram would be summed up and converted subsequently into the probabilities of 1-, 3- and 5-year CSS which were parallel lines below the figure with linear relationship scales with each other. It was shown in the nomogram that the pathological grade has the greatest influence on the CSS probability for US, followed by age at diagnosis, surgery status, SEER stage, AJCC stage, histological grade, chemotherapy status, insurance record, tumor size, race, radiotherapy status, and finally marital status.

Nomogram Comparison And Evaluation

Next, we applied a series of indicators to evaluate the performance of the new prediction model underpinning it. We found that this nomogram provided relatively higher C-indexes than for the AJCC 7th edition staging system in both the training cohort (0.796 vs. 0.706) and the validation cohort (0.767 vs. 0.713), indicating that the new model had better discriminative ability. Furthermore, the ROC curves for the training cohort showed that the AUC values were significantly larger for the nomogram (0.842, 0.845,0.860 at 1,3,5-year, respectively) than for the AJCC staging system (0.755, 0.772, and 0.774, respectively). Likewise, the ROC curves for the validation cohort demonstrated that the AUC values were significantly larger for the nomogram (0.833 at 1-year, 0.798 at 3-year, and 0.797 at 5-year) than for the AJCC staging system (0.763, 0.741, and 0.747, respectively) (Fig. 3).

Validation And Calibration Of The Nomogram

The NRI values for the 1-, 3- and 5-year CSS rates in the training cohort were 64.6% (95% confidence interval [CI] = 55.3–73.5%), 59.0% (95% CI = 50.7%-67.9%) and 62.2% (95% CI = 52.8–71.4%), respectively, and in the validation cohort, 47.2% (95% CI = 25.0-63.1%), 37.6% (95% CI = 14.1–51.4%) and 29.9% (95% CI = 7.4–55.0%), respectively. These values indicated that the nomogram provided exceedingly superior predictive performance compared with the AJCC staging system. Likewise, the IDI values for the 1-, 3- and 5-year CSS rates in the training cohort were 8.64, 9.63 and 9.50%, respectively, and 3.98, 5.79 and 5.88% in the validation cohort (all $p < 0.001$). These results further suggested that the predictive power of the new model was significantly improved to that of the AJCC model.

Calibration plots of the nomogram showed that the predicted curves of 1-, 3- and 5-year CSS probabilities for the training and validation cohorts were nearly identical to the actual observations, which demonstrated that the new model had great calibration ability (Fig. 4).

Clinical Usefulness

Finally, we used DCA to evaluate the clinical effectiveness of the model. With the threshold probability as the abscissa and the net benefit as the ordinate graphically, the plots of the 1-, 3- and 5-year DCA curves indicated that the DCA curves showed a larger net benefits of the new model in both the training and validation cohorts compared with the AJCC staging system (Fig. 5), which indicated that the new model was clinical beneficial and would have a positive effect on practical decision making.

Discussion

Uterine sarcoma is a group of rare gynecologic tumors with various natures, aggressive progress, and different lines of treatment [3]. Most of them have a poor outcome. Up to now, there is no efficient prognostic staging system that could help to estimate CSS at diagnosis in US patients.

Nomogram, as a statistical tool, can provide the most accurate predictions by a simple graphical presentation. This convenient nomogram could provide accurate individualized predictions for specified points. Recently it had been developed for several cancers such as NSCLC hepatocellular carcinoma(HCC), and adult skin melanoma[16,17,18]. However, few nomograms have been constructed for US patients. Zhou *et al* identified 6-gene-based prognostic signature for US [19]. Li *et al* evaluated the benenit of adjuvant radiotherapy for uterine leiomyosarcoma and carcinosarcoma [20]. The latest and largest study done by Mona Hosh *et al* identified 13089 cases of uterine sarcoma diagnosed from 2000 to 2012 [10]. To our knowledge, this study was the first time to develop a comprehensive prognostic nomogram to predict the 1-, 3-, and 5-year CSS for US based on the SEER database.

Pathological grade, age, surgery, AJCC stage, SEER stage,, histological differentiation, chemotherapy, insurance record, tumor size, ethnicity, radiotherapy and marital status were identified as the prognostic factors of the CSS through multivariate Cox regression. Among them, the most notable depressed prognosis for CSS of US patient is pathological grade. It was revealed that the survival rates of patients with grade III and IV were worse compared to those grade I patients, which was consistent with previous studies [21]. However, it had no significant differences between patients of grade III and grade IV.

Age at diagnosis played the secondary crucial role in our model, although the exact mechanism remained unclear. Mona Hosh *et al* also found that the incidence of US increased with increasing age, while aged 50 years or older patients had worse survival than those younger patients [10]. Several reports have shown that the elder patients did not derive the same benefit from cancer treatments as the general population in clinical trials, which might because of the declines of organ function. The present study indicated that black US patient, tumor size (> 5.0 cm) and histological type were all associated with poor prognosis for patients with US. Other studies also indicated that progression and poor survival rates were more common in patients with black, carcinosarcoma and larger tumors [22].

More interestingly, we discovered the marital status influenced CSS of Uterine Sarcoma for the first time. Evidences showed that unmarried patients exhibited shorter OS and CSS compared with married patients in lung and liver cancer [24,23]. In the present study, patients of Separated, Divorced and Widowed (SDW) had the worst survival compared to those married patients, followed by the single patients. This might

because that marriage could relieve a patient of the depression and anxiety caused by cancer, for a spouse can share the emotional burden and provide strong social support [25]. Insurance was also strongly associated with the prognosis of uterine sarcoma. Patients with insurance could receive better medical support, less economical and less psychological distress compared with uninsured patients. These new information could therefore further help clinicians to make more effective clinical decisions.

Surgery status, SEER stage, AJCC stage, radiotherapy status were also found to affect the survival probability. Surgery is the gold standard treatment for US [2]. In addition, among these clinical parameters, the surgery status had the highest discriminating power in our study Another important factor was the localized stage of US at initial diagnosis. The patients that had distant metastatic have more aggressive disease than whose only had localized disease.

Radiation therapy is usually performed in advanced uterine sarcoma patients. Several retrospective researches have suggested radiotherapy after surgery could decrease pelvic recurrence, but not for distant metastases [26]. In contrast, Wong *et al* found that adjuvant pelvic radiotherapy might improve OS and reduce local recurrence for leiomyosarcoma [27]. In our study, Fig. 2 clearly showed both surgery and radiotherapy could improve the survival on the 1-, 3-, and 5-year CSS probabilities in US patients.

Notably, we identified chemotherapy provides patients with a better prognosis for the first time. There are very few studies focusing on chemotherapy and patient prognosis for US patients in SEER database. Efficacious chemotherapy to achieve prolonged survival in those with both early and advanced-stage US patients has been elusive. Hensley et al evaluated the role of 4 cycles of gemcitabine and docetaxel in 25 high-grade uterine leiomyosarcima patients, and found that prolonged PFS and OS than before [28]. However, Littell *et al* compared gemcitabine-docetaxel verus obesevation in 110 stage I uLMS patients after surgery, and found no significance difference in disease-free or OS or recurrence in two groups [29]. Our nomogram showed that chemotherapy had an even higher discriminating power than radiotherapy. This data on chemotherapy could help clinicians to choose individualized adjuvant treatment after surgery.

To further assess whether our nomogram was superior to the traditional AJCC staging system, NRI, IDI, DCA, discrimination and calibration were used to evaluate the performance of our survival model. The survival nomogram performed better discrimination with C-indexes of 0.796, 0.767 for the training and validation cohort, as the values only 0.706 and 0.713 for the AJCC staging system. As shown in Fig. 3, for both training and validation cohort, all the 1-, 3-, and 5-year AUC values of the AJCC staging system were significant lower than those of the nomogram. The plots resembling 45-degree lines indicatedthe predictions of our nomogram were well calibratedFurthermore, the NRI and IDI both demonstrated that the new nomogram improved the predictive ability than the AJCC staging system. Then we applied the DCA curves to assess the clinical effectiveness of the nomogram. Our results showed that the 1-, 3-, and 5-year DCA curves for CSS exhibits better clinical effectivenss for predicting survival compared to the traditional AJCC staging system in both training and validation cohorts.

This study was based on data from the SEER database, but of course, it still had several limitations. First, adjuvant hormonal therapy was not included in this nomogram, which might be due to the hormonal therapy was not routinely recommended as postoperative treatment in all histological types of US. Second, SEER database did not use the FIGO staging system for US patients,instead the SEER stage and AJCC stage were used. Third, some potential predictive variable such as serum marker, neutrophil-to-lymphocyte ratio were not included in this study because of these datas' absence in the SEER detabese. Forth, our study excluded the patients diagnosed after 2015. The NCCN guideline of Uterine Neoplasms modified the pathology types of uterine sarcoma since 2016. More recently diagnosed patients and patients of several rare pathological types were excluded to make sure sufficient follow-up so that we could adequately assess the association of treatment with survival.

Conclusions

In summary, we have developed and validated a novel nomogram to predict the 1-, 3-, and 5-year CSS for US based on a population-based database. Our nomogram is better than the AJCC staging system, and could be used as a valuable tool to help clinicians to provide more individualized treatment and individualized survival prediction in clinical practice.

Abbreviations

US
Uterine sarcoma; CSS:Cancer-specific survival; AJCC:American Joint Committee on Cancer; SEER:Surveillance, Epidemiology, and End Results database; C-index:Concordance index; AUC:Area under the curve; NRI:Net reclassification improvement; IDI:Integrated discrimination improvement; DCA:Decision-curve analysis; HR:Hazard ratio.

Declarations

Acknowledgements

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Conflict of Interest

All authors declare that they have no conflict of interests.

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Authors' contributions

Yuan-jie Li and Jun Lyu contributed equally to the work.

Yuan-jie Li and Jun Lyu analyzed the data and performed the conceptualization and formal analysis. Chen Li performed statistical analysis and data interpretation. Hai-rong He and Jin-feng Wang were responsible for the quality control of data and data extraction. Yue-ling Wang contributed to the writing-review and editing. Jing Fang performed investigation, literature research. Jing Ji designed the study and submitting manuscript. All authors contributed to writing of the manuscript and approved the final version.

Ethics approval and consent to participate

This study was exempted from Institutional Review Board approval, in view of the SEER's use of unidentifiable patient information. Due to the strict register-based nature of the study, informed consent was waived.

Consent for publication

No applicable.

Availability of data and materials

Data from the SEER program is available for public. The data supporting the conclusions of this article are available in the Surveillance Epidemiology, and End Results (SEER) database (https://seer.cancer.gov/).

Competing interests

All the authors declare that they have no competing interests.

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Figures

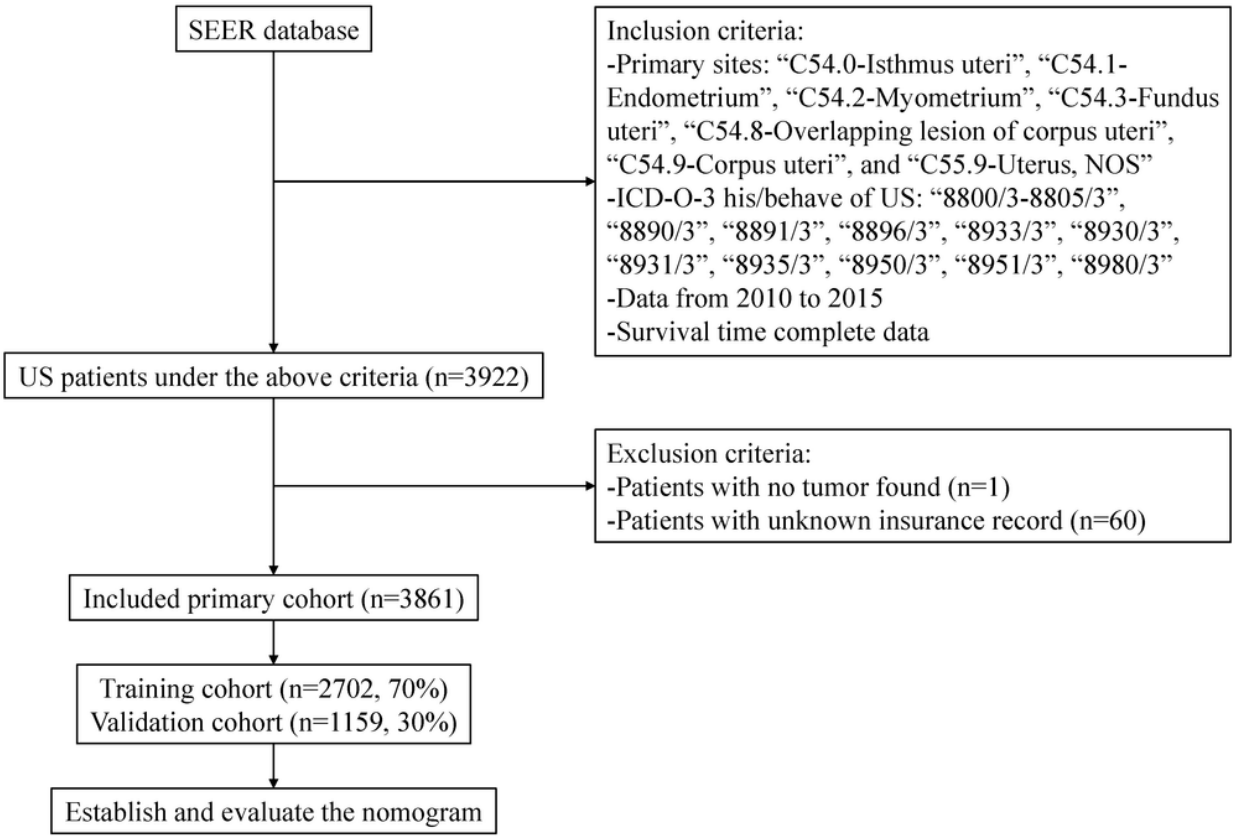

Figure 1

Research flowchart

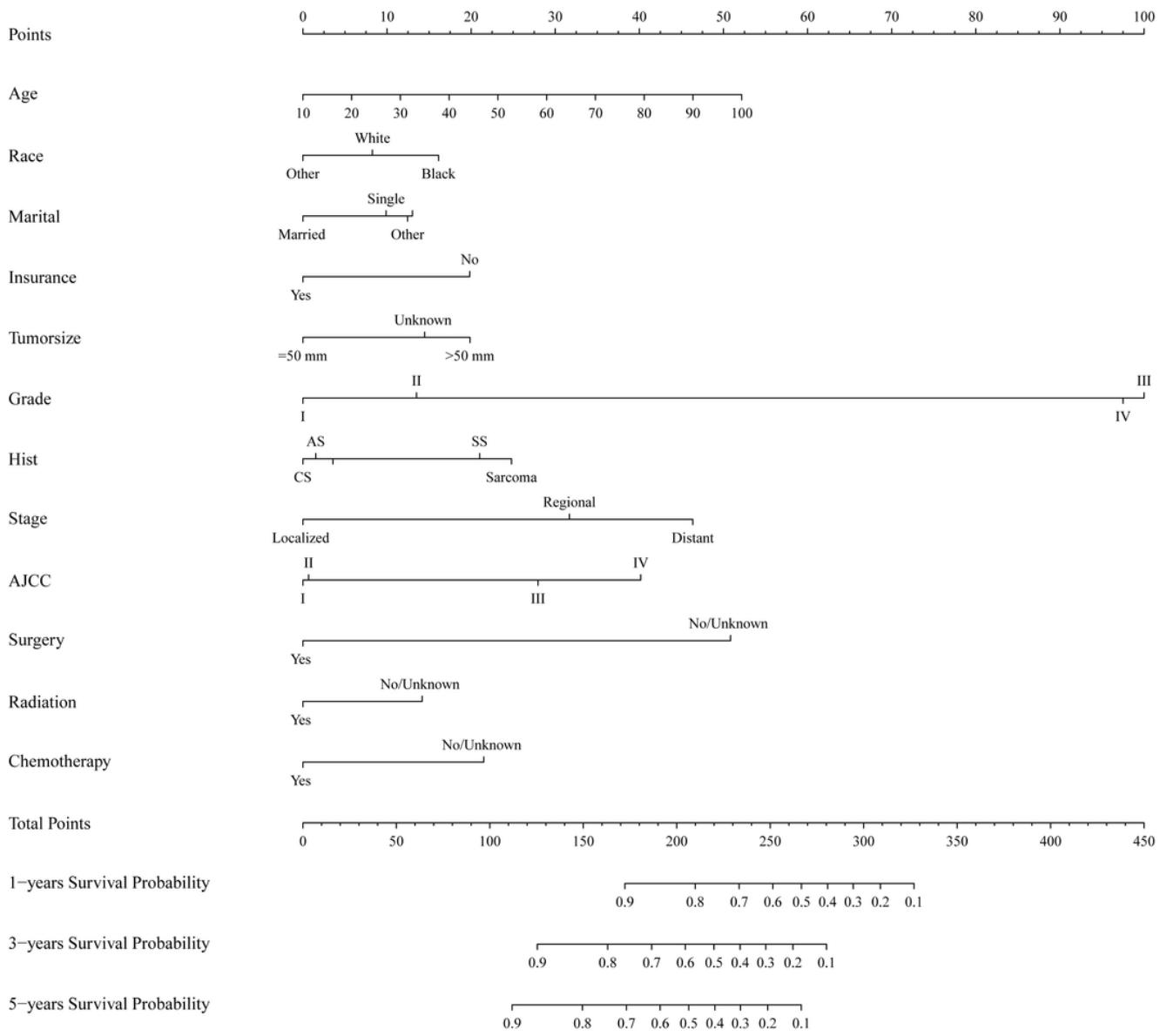

Figure 2

Nomogram predicting 1-, 3- and 5-year survival. AJCC, 7th AJCC tumor stage.

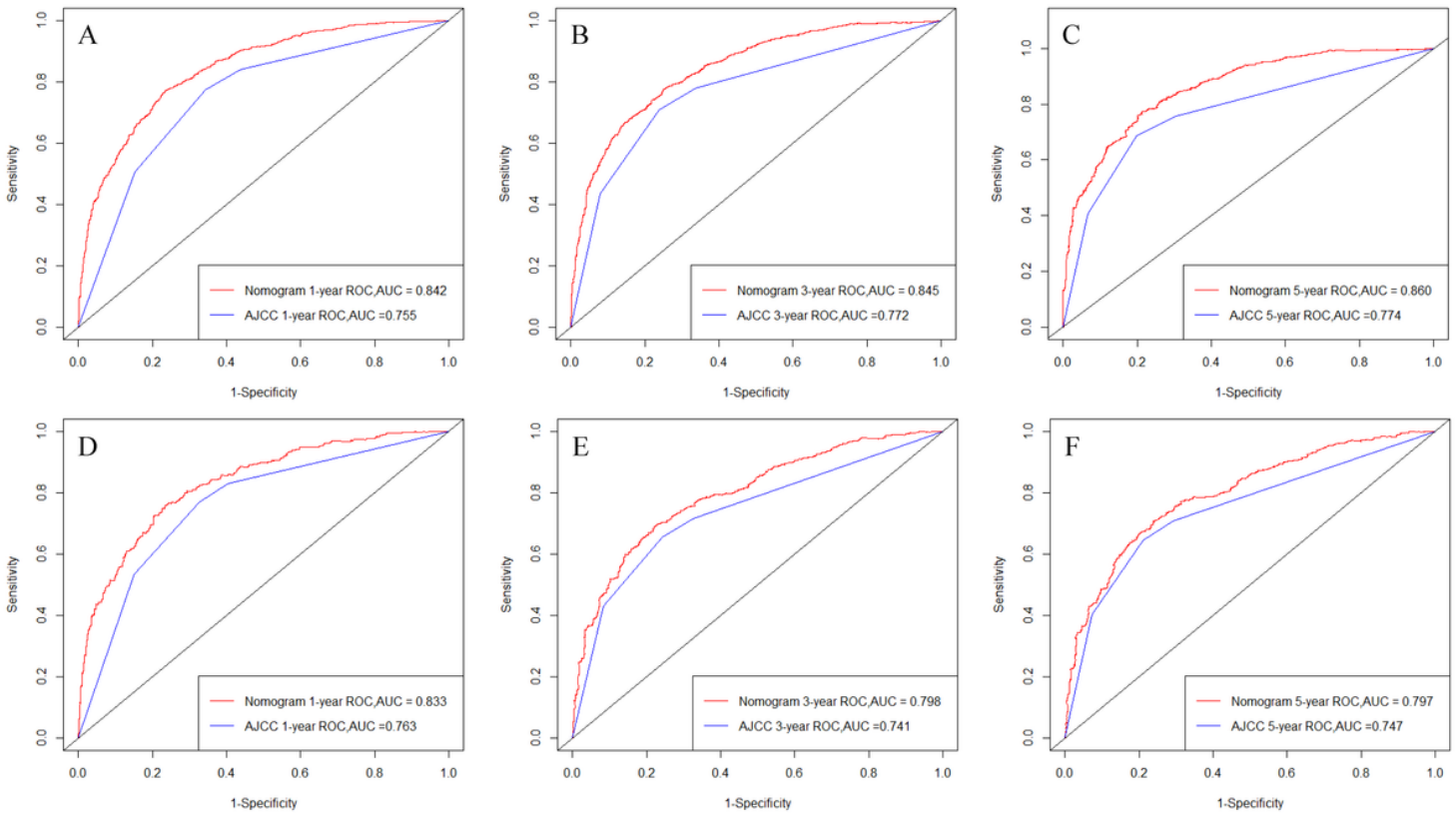

Figure 3

ROC curves. ROC curve analyses were generated to test the performance evaluating between the new model and the traditional AJCC model, by the AUC. A, B and C came from the training set, D, E, and F came from the validation set.

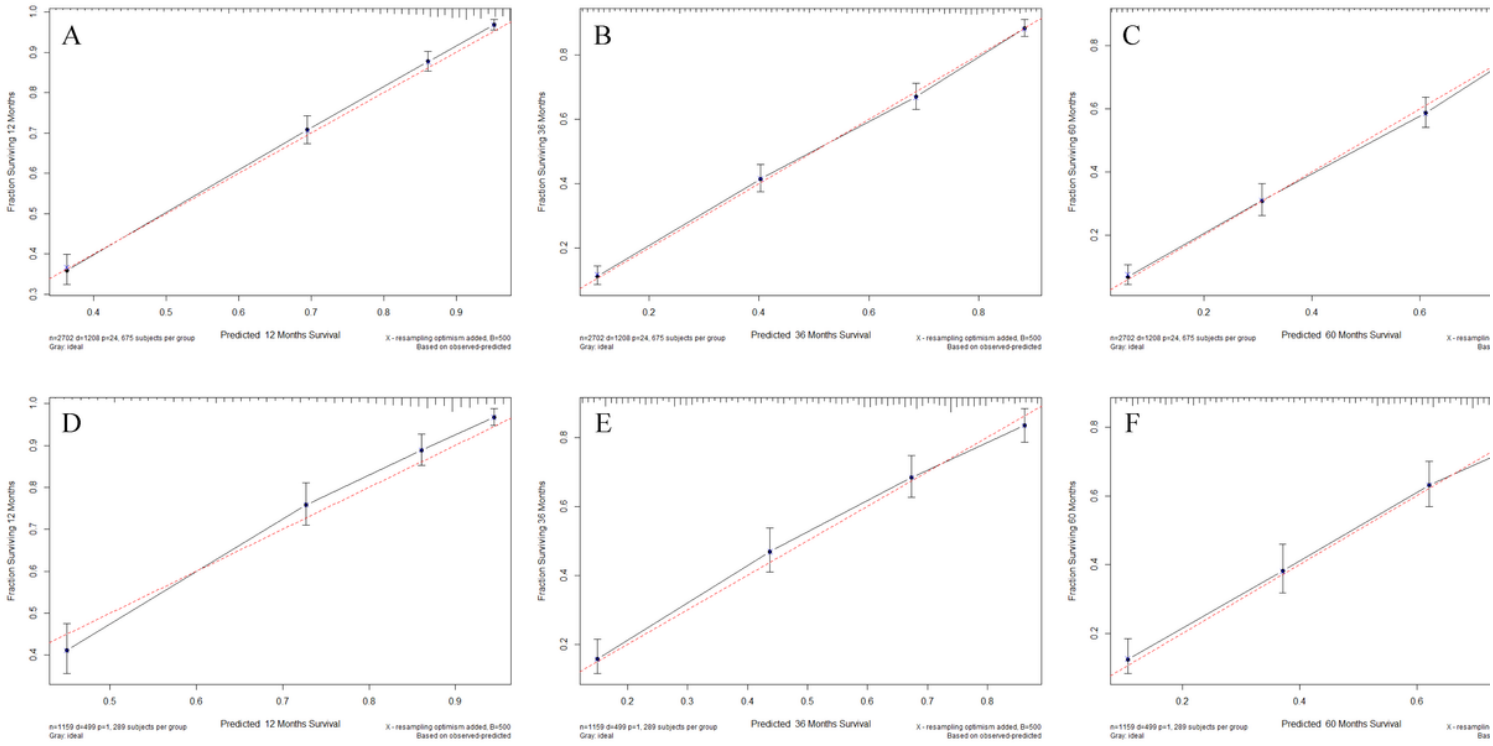

Figure 4

Calibration curves. Calibration curves for 1-, 3- and 5-year CSS depict the calibration of each model in terms of the agreement between the predicted probabilities and observed outcomes of the training cohort (A,C,E) and validation cohort (B,D,F).

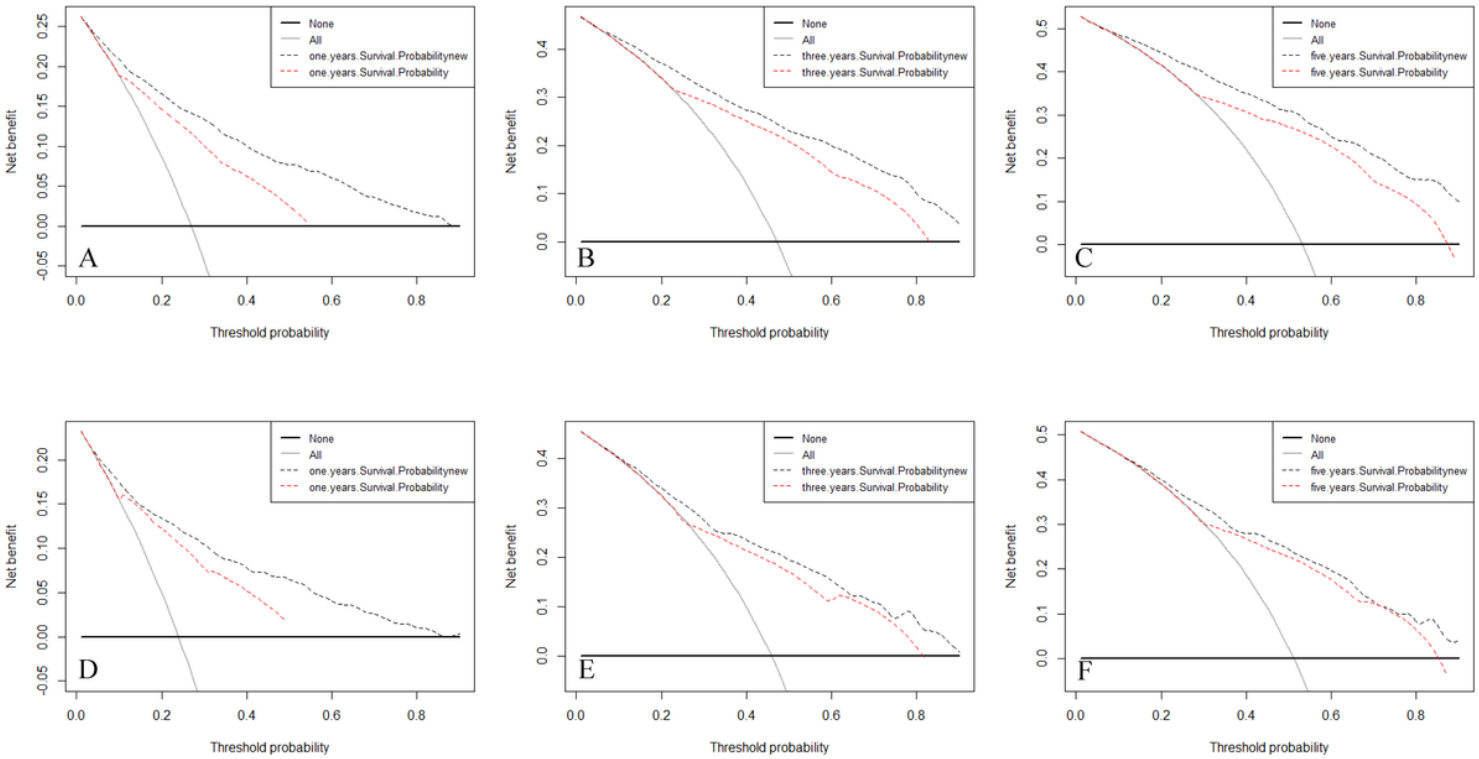

Figure 5

Decision curve analysis curves. Decision curve analysis of the training (A,B,C) and validation cohorts (D,E,F)