

# Novel nomograms individually predict the survival of patients with soft tissue sarcomas after surgery

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**Background:** The aim of the study was to build and validate practical nomograms to better predict the overall survival (OS) and cancer-specific survival (CSS) of the patients with soft tissue sarcomas (STS) who underwent surgery.

**Methods:** Patient data were extracted from the Surveillance, Epidemiology, and End Results (SEER) database. We identified 8804 patients who underwent surgery with STS between 2007 and 2015, and randomly divided them into the training (n=6164) and validation (n=2640) cohorts. The Cox regression analysis and cumulative incidence function were performed to identify the independent prognostic factors associated with OS and CSS, respectively. The performance of the nomograms was evaluated using Harrell's concordance index (C-index) and the calibration curves. Decision curve analysis (DCA) was introduced to compare the clinical practicality between the nomograms and the AJCC staging system.

**Results:** Eight independent prognostic factors for OS and seven for CSS were determined and then used to build the nomograms for 3- and 5-year OS and CSS, respectively. The C-indexes of the nomograms for predicting OS were 0.788 in the internal validation and 0.823 in external validation, significantly higher than C-index of the AJCC staging system ( $P<0.001$ ). The similar results were obtained in the validation cohort. Internal and external calibration curves for the predicting 3- and 5-year OS and CSS showed excellent agreement between the prediction and the actual survival outcomes. In addition, DCA demonstrated that our nomograms were superior over the AJCC staging system with obtaining more clinical net benefits.

**Conclusions:** We established and validated the nomograms that could accurately predict the 3- and 5-year OS and CSS for STS patients who underwent surgery. The nomograms showed more robust and applicable performance than the AJCC staging system for predicting OS and CSS.

**Keywords:** SEER, soft tissue sarcomas, prognosis, nomogram, decision curve analysis

## Introduction

Soft tissue sarcomas (STS) are a group of rare solid tumors and accounts for around 1% of all malignancies.<sup>1</sup> In 2018, an estimated 13,040 new cases will be diagnosed in the United States, with nearly 5,150 mortalities.<sup>2</sup> It constitutes highly heterogeneous tumors of mesodermal origin with distinct clinicopathological features. And thus STS patients' prognosis varies extremely. Surgical resection combined with radiotherapy is the current management for STS patients. Despite the great advances in diagnostic techniques and therapies, the overall prognosis of STS remains poor.<sup>3</sup>

The American Joint Commission on Cancer (AJCC) tumor-node-metastasis (TNM) staging systems, representing the gold standard classification system for STS,<sup>4</sup> only takes into consideration the tumor size, nodal involvement, and distant

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metastases. However, studies have demonstrated that it does not provide sufficient details to encompass the diversity of STS and should be improved.<sup>5,6</sup> Additionally, several other important factors such as age, race, tumor size, tumor differentiation, and socioeconomic status have also significant influences on the survival of STS patients. Ignoring these significantly survival-associated parameters would be unfavorable to survival prediction. Therefore, there is an urgent need to develop a comprehensive prognostic evaluation model considering both tumor characteristics and patient status in clinical practice.

Nomogram, as simple mathematical models for prediction, has widely used to predict cancer prognosis. Compared with the AJCC TNM staging system, nomograms can more accurately estimate survival for individual patients by integrating important prognostic variables.<sup>7–9</sup> Since STS is very rare and histological heterogeneous, most analyses of prognostic factors are mainly from retrospective, single-center with small sample.<sup>10–13</sup> To our knowledge, no nomogram has been built based on STS patients treated with surgery on the basis of population-based data. Therefore, we aimed to build and validate the first two nomograms for predicting OS and CSS for STS patients who underwent surgery based on population-based data in the Surveillance, Epidemiology, and End Results (SEER) database.

## Materials and methods

### Patients

Data about STS patients with surgical treatment were extracted from the SEER database (2007–2015), using the SEER\*Stat software version 8.3.2<sup>1,4</sup>. The inclusion criteria for the eligible patients were as follows: 1) STS was histologically diagnosed as the first and only primary tumor; 2) Patients older than 18 years old; 3) Demographic and clinicopathologic information were complete and detailed, and the follow-up was complete with known survival outcome. Patients were excluded if their diagnostic information was obtained only from a death certificate or autopsy report, as well as their survival time was less than 1 month. To construct and validate the nomogram, all STS patients were randomly divided into a training cohort (n=6164, 70%) and validation cohort (n=2640, 30%). Institutional review board approval was not demanded in our study for SEER database is publicly available and we get access to it via accession number: 10165-Nov 2017.

### Study variables

The demographic and clinicopathologic data for each patient were extracted from the SEER database, including age, sex, race, marital status, median household income, and insurance status, tumor size, histologic subtype, grade, SEER stage, survival months, vital status and causes of death. The continuous variables including age and tumor size were converted to categorical variable according to optimal cut-offs, which were determined by X-tile program. (Age,  $\leq 60$  years, 60–75 years,  $> 75$  years; tumor size,  $\leq 5$  cm, 5–10 cm,  $> 10$  cm). The race consisted of white, black and others (American Indian/AK Native, Asian/Pacific Islander). Marital status was described as married, unmarried (single, divorced or widowed); insurance status, as insured and uninsured. Histologic subtypes were grouped as follows: liposarcoma, leiomyosarcoma, fibromyxosarcoma, malignant fibrous histiocytoma, hemangiosarcoma, malignant peripheral nerve sheath tumor, synovial sarcoma, rhabdomyosarcoma, undifferentiated sarcoma, and other sarcomas.

## Statistical analysis

### Construction of the nomograms

The training cohort was used to build the nomograms. One of the primary endpoints in our study was OS, which was calculated as the time from diagnosis to death due to any cause or censoring. The Kaplan–Meier method and log-rank test were applied in the univariate analysis. Variables significantly related with survival ( $P < 0.05$ ) in univariate analysis were subsequently subjected to the multivariable Cox regression analysis. Next, the independent prognostic factors determined in the multivariate Cox analysis were integrated to build the nomograms for OS.

The other primary endpoint was CSS, which was calculated as the time from diagnosis to death from STS. When building the competing risks nomograms for CSS, death from other causes was counted as a competing event. The cumulative incidence function was used to predict the probability of death from STS and other causes, respectively. Variables with  $P$ -values  $< 0.001$  in the Gray's test were significant independent prognostic factors for CSS. By combining these factors, we built the competing risks nomograms for 3- and 5-year CSS in STS patients.<sup>15</sup>

### Validation of the nomograms

The validations were performed both internally (in the training cohort) and externally (in the validation cohort),

**Table 1** Patient demographics and clinicopathological characteristics

Characteristic	Total (n=8804)	Training cohort (n=6164)	Validation cohort (n=2640)
	N (%)	N (%)	N (%)
Sex			
Female	3950 (44.9)	2758 (44.7)	1192 (45.2)
Male	4854 (55.1)	3406 (55.3)	1448 (54.8)
Age(year)			
≤60	5088 (57.8)	3557 (57.7)	1531 (58.0)
60–75	2471 (28.1)	1728 (28.0)	743 (28.1)
>75	1245 (14.1)	879 (14.3)	366 (13.9)
Race			
Black	906 (10.3)	625 (10.1)	281 (10.6)
White	7089 (80.5)	4972 (80.7)	2117 (80.2)
Others	809 (9.2)	567 (9.2)	242 (9.2)
Marital status			
Married	5211 (59.2)	3649 (59.2)	1562 (59.2)
Unmarried	3593 (40.8)	2515 (40.8)	1078 (40.8)
Insurance status			
Insured	7266 (82.5)	5080 (82.4)	2186 (82.8)
Uninsured	1538 (17.5)	1084 (17.6)	454 (17.2)
Tumor size(cm)			
≤5	2485 (28.2)	1719 (27.9)	766 (29.0)
5–10	2525 (28.7)	1741 (28.2)	784 (29.7)
>10	3794 (43.1)	2704 (43.9)	1090 (41.3)
Histologic subtype			
Liposarcoma	2898 (32.9)	2055 (33.3)	843 (31.9)
Leiomyosarcoma	1257 (14.3)	881 (14.3)	376 (14.2)
Fibromyxosarcoma	789(9.1)	570(9.2)	228 (8.6)
MFH	580 (6.6)	396 (6.4)	185 (7.0)
Hemangiosarcoma	162 (1.8)	109 (1.8)	53 (2.0)
MPNST	322(3.7)	234 (3.8)	88 (3.3)
Synovial sarcoma	414 (4.7)	279 (4.5)	135 (5.1)
Rhabdomyosarcoma	149 (1.7)	112 (1.8)	37 (1.4)
Undifferentiated sarcoma	327(3.7)	233 (3.8)	94 (3.6)
Other	1897 (21.5)	1296 (21.0)	601 (22.8)
Grade			
I	2056 (23.4)	1443 (23.4)	613 (23.2)
II	1703 (19.3)	1200 (19.5)	503 (19.1)
III	1999 (22.7)	1393 (22.6)	606 (23.0)
IV	3046 (34.6)	2128 (34.5)	918 (34.8)
SEER stage			
Localized	5988 (68.0)	4189 (68.0)	1799 (68.1)
Regional	2160 (24.5)	1521(24.7)	639 (24.2)
Distant	656 (7.5)	454 (7.4)	202 (7.7)

(Continued)

**Table 1** (Continued).

Characteristic	Total (n=8804)	Training cohort (n=6164)	Validation cohort (n=2640)
	N (%)	N (%)	N (%)
Survival outcomes			
Alive	6515 (74.0)	4548 (73.8)	1967 (74.5)
Death from STS	1797 (20.4)	1273 (20.7)	524 (19.8)
Death from other causes	492 (5.6)	343 (5.5)	149 (5.7)

**Abbreviations:** Others, American Indian/Alaska Native/Asian/Pacific Islander; MFH, malignant fibrous histiocytoma; MPNST, malignant peripheral nerve sheath tumor; SEER, Surveillance, Epidemiology, and End Results.

using C-index and calibration curve. A total of 1000 bootstrap resamples were used in both validations. The marginal estimate versus model average predictive probability was applied to plot calibration curves, representing the calibration between the prediction by nomogram and the actual survival outcome. In an excellently calibrated nomogram, the prediction would fall on a 45-degree diagonal. The C-index refers to the probability of concordance between the predictions and the actual survival outcome, with value fluctuating between 0.5 (no discrimination) and 1.0 (excellent discrimination).<sup>16</sup>

## Decision curve analysis

Decision curve analysis (DCA) is a novel method for determining whether alternative diagnostic and prognostic systems have more net clinical benefits compared with other commonly used strategies. In this study, we conducted DCA to compare the clinical practicality and benefits between nomograms and the AJCC staging system in both the training and the validation cohort.

All statistics analyses were performed by R software (version 3.3.0). the R packages used in our study included survminer, rms, cmprsk, and rcorrcens. All statistical tests were two-sided, and *P*-value less than 0.05 was statistically significant.

## Results

### Demographic and clinicopathological characteristics of STS patients

A total of 8,804 eligible STS patients who underwent surgery diagnosed between 2007 and 2015 in the SEER database were included. Of those patients, 6,164 patients were

**Table 2** Univariate and multivariate analysis of OS in the training cohort

Variables	Univariate analysis		Multivariate analysis	
	Log Rank $\chi^2$	P	HR(95% CI)	P
<b>Sex</b>	9.8	0.002	Reference	<0.001
Female			1.22	
Male			(1.10–1.35)	
<b>Age (year)</b>	307	<0.001	Reference	<0.001
≤60			1.56	
60–75			(1.38–1.76)	
>75			3.20	<0.001
			(2.81–3.64)	
<b>Race</b>	0.7	0.800	-	-
Black			-	
White			-	
Others			-	
<b>Marital status</b>	20.9	<0.001	Reference	0.031
Married			1.14	
Unmarried			(1.02–1.26)	
<b>Insurance status</b>	37.3	<0.001	Reference	<0.001
Insured			1.34	
Uninsured			(1.18–1.53)	
<b>Tumor size (cm)</b>	195	<0.001	Reference	<0.001
≤5			1.48	
5–10			(1.23–1.78)	
>10			2.47	<0.001
			(2.07–2.95)	
<b>Histologic subtype</b>	292	<0.001	Reference	0.002
Fibromyxosarcoma			1.44	
Leiomyosarcoma			(1.13–1.82)	
Liposarcoma			1.12	0.324
			(0.89–1.40)	
MFH			1.52	0.001
			(1.19–1.94)	
Hemangiosarcoma			4.41	<0.001
			(3.10–6.10)	
MPNST			2.32	<0.001
			(1.73–3.12)	
Synovial sarcoma			1.39	0.041
			(1.01–1.90)	

(Continued)

**Table 2** (Continued).

Variables	Univariate analysis		Multivariate analysis	
	Log Rank $\chi^2$	P	HR(95% CI)	P
Rhabdomyosarcoma			1.63	0.006
			(1.15–2.33)	
Undifferentiated sarcoma			1.35	0.561
Other			(0.99–1.85)	
			1.49	<0.001
			(1.19–1.86)	
<b>Histologic grade</b>	496	<0.001	Reference	<0.001
I			1.72	
II			(1.36–2.16)	
III			2.82	
			(1.95–4.08)	
IV			2.84	<0.001
			(1.97–4.10)	
<b>SEER stage</b>	970	<0.001	Reference	<0.001
Localized			1.45	
Regional			(1.29–1.62)	
Distant			4.54	<0.001
			(3.97–5.19)	

**Abbreviations:** Others, American Indian/Alaska Native/Asian/Pacific Islander; MFH, malignant fibrous histiocytoma; MPNST, malignant peripheral nerve sheath tumor; SEER, Surveillance, Epidemiology, and End Results.

randomly assigned to the training cohort and 2,640 were to the validation cohort. In the whole cohort, the median age was 57.0 years (range:18–94 years) with a male-to-female ratio of approximately 1:1. The majority of STS patients were younger (57.8%), white (80.5%), insured (82.5%), and have localized SEER stage (68.0%). The median follow-up time was 31 months (range:13–107 months). At the end of follow up, 2,289 (36.0%) patients had died, with 1,797 (20.4%) deaths from STS and 492 (5.6%) deaths from other causes. The descriptive analysis of patient characteristics is shown in Table 1.

## Nomograms predicting 3- and 5-year survival

In the training cohort, eight factors were identified as the independent prognostic factors according to the univariate and multivariate analyses (Table 2). These variables were age, sex, marital status, insurance status, tumor size, histologic subtype, histologic grade, and SEER stage. A nomogram based on the above variables was developed

to estimate 3- and 5-year OS for STS patients with surgical treatment (Figure 1A). Estimates of cumulative incidences of death from CSS by clinicopathological variables are listed in Table 3. The main variables significantly associated with CSS were age, sex, insurance status, tumor size, histologic subtype, histologic grade, and SEER stage ( $P<0.001$ ). A second nomogram predicting CSS was established using these variables (Figure 1B).

Using a nomogram to predict survival is simple. First, to include the relevant prognostic factor, a vertical line should be drawn from every factor to the “Points” line of nomogram. Then, the total scores are obtained and project them to the “Total Points” to get the patient’s probabilities of survival. To clarify, we took two STS patients, for example, a 65-year-old married man was diagnosed with liposarcoma (grade III, tumor size of 6.0 cm); he had insurance. By adding the points, he would score 118 points, which indicated that he has 86% probability of OS at the three year. However, for a 76-year-old unmarried female patient with hemangiosarcoma (grade IV, tumor size of 11.0 cm), who had no insurance, the total score would be 320 points; thus, her probability of OS at the three year would be well below 10%.

## Nomogram validation

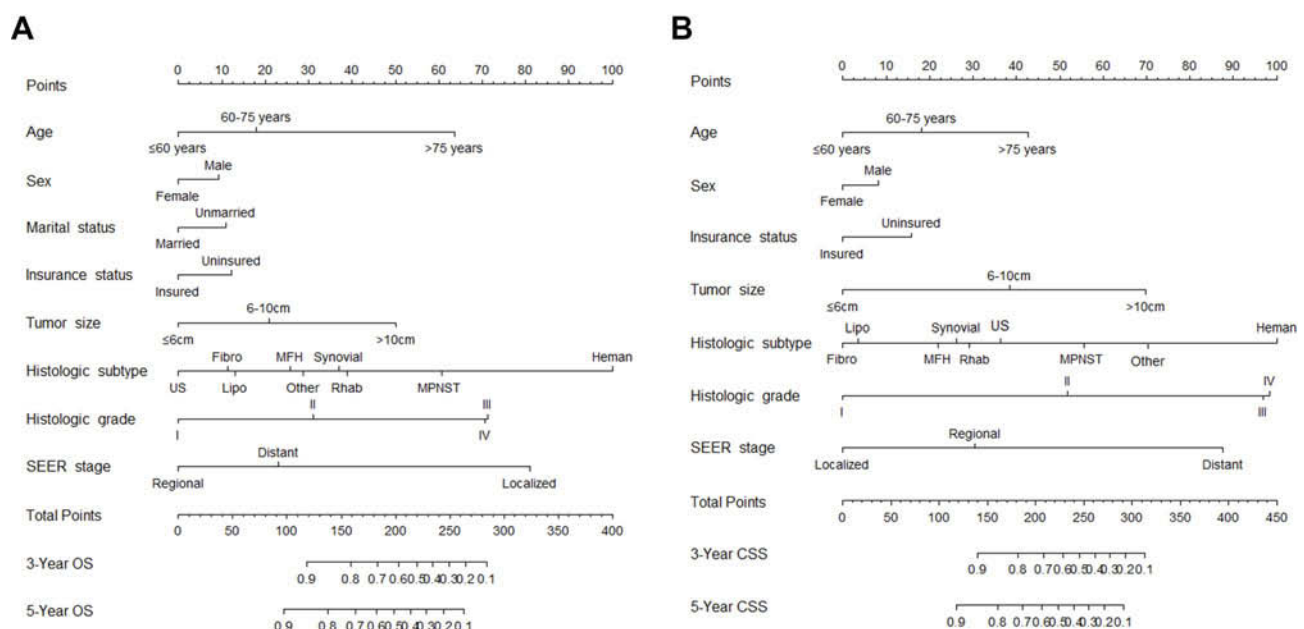
Internal validation through the training cohort showed that the C-indexes for the nomograms in predicting OS and

CSS was 0.788 and 0.827, respectively. Similarly, in the external validation, the C-indexes for prediction of OS and CSS were 0.823 and 0.833, respectively. The internal and external calibration curves were shown in Figures 2 and 3, respectively, indicating excellent agreement between the nomograms prediction and actual survival outcomes.

Additionally, a comparison between our nomograms and the AJCC staging system in predicting OS/CSS was performed. In the training cohort, the C-indexes of the nomograms we established for predicting OS and CSS were obviously higher than that of the AJCC staging system (C-index for OS, 0.788 vs 0.722,  $P<0.001$ , C-index for CSS, 0.827 vs 0.755,  $P<0.001$ ). Moreover, our nomograms also displayed more powerful efficiency of discrimination in the validation cohort compared with the AJCC staging system (C-index for OS, 0.823 vs 0.731,  $P<0.001$ , C-index for CSS, 0.833 vs 0.770,  $P<0.001$ ).

## Decision curve analysis

In the training cohort, our nomograms obtained more net benefits than the AJCC system within wide threshold probabilities, which indicated that the nomograms had good clinical applicability. For example, compared with the AJCC system, with a threshold probability of 0.4, our nomogram in predicting OS and CSS could obtain an increased net clinical benefit of 0.036, 0.015, respectively, (Figure 4A and B). Furthermore, when performing DCA in



**Figure 1** Nomograms for predicting 3- and 5-year (A) OS and (B) CSS for STS patients treated with surgery.

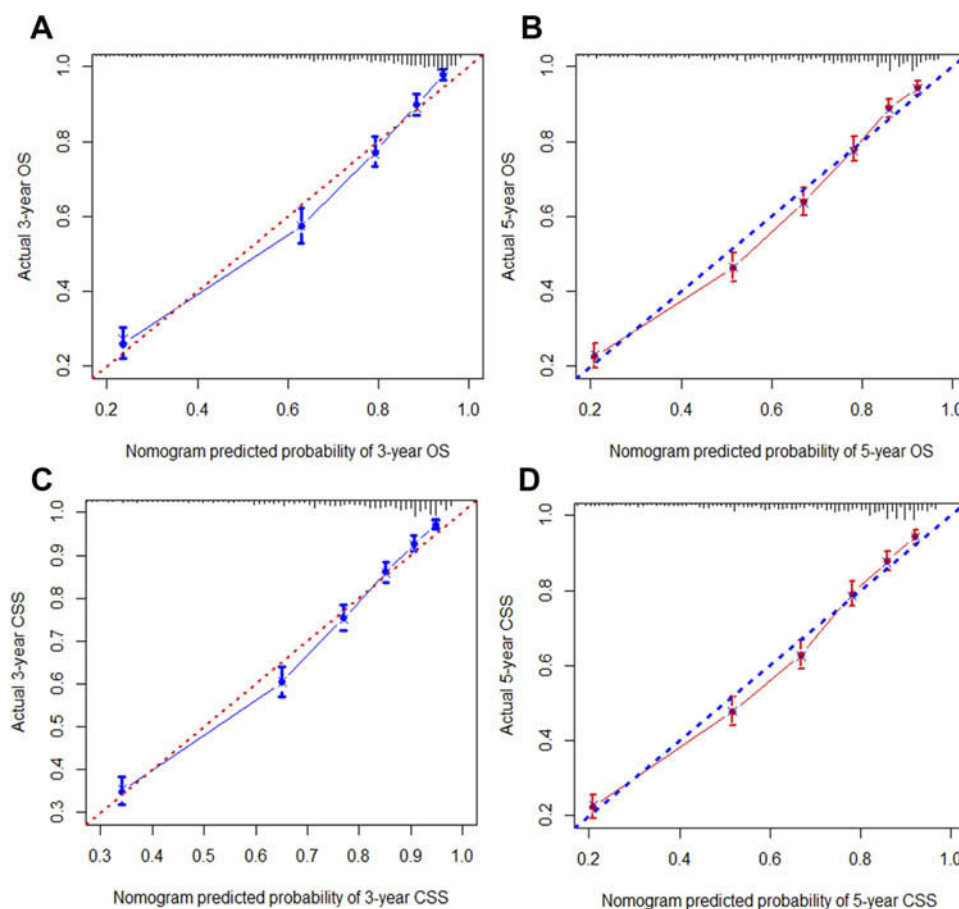
**Abbreviations:** Fibro, fibromyxosarcoma; Heman, hemangiosarcoma; Lipo, liposarcoma; MFH, malignant fibrous histiocytoma; MPNST, malignant peripheral nerve sheath tumor; Rhab, rhabdomyosarcoma; Synovial, synovial sarcoma; US, undifferentiated sarcoma.



**Table 3** The 3- and 5-year cumulative incidences of death resulting from CSS among STS patients treated with surgery in the training cohort

Variables	Cause-specific death			Death from other causes		
	3-year (%)	5-year (%)	P	3-year (%)	5-year (%)	P
<b>All Patients</b>	0.208	0.269	0.045	0.043	0.068	0.016
<b>Sex</b>						
Female	0.196	0.256		0.038	0.058	
Male	0.217	0.279		0.046	0.075	
<b>Age (year)</b>			<0.001			<0.001
≤60	0.181	0.237		0.016	0.024	
60–75	0.226	0.293		0.049	0.072	
>75	0.278	0.349		0.134	0.224	
<b>Race</b>			0.389			0.072
Black	0.229	0.272		0.061	0.072	
White	0.204	0.265		0.042	0.036	
Others	0.214	0.302		0.026	0.070	
<b>Marital status</b>			0.261			<0.001
Married	0.194	0.258		0.033	0.055	
Unmarried	0.229	0.286		0.057	0.086	
<b>Insurance status</b>			<0.001			0.445
Insured	0.245	0.312		0.044	0.074	
Uninsured	0.324	0.393		0.053	0.071	
<b>Tumor size (cm)</b>			<0.001			0.449
≤5	0.093	0.125		0.046	0.068	
5–10	0.199	0.275		0.033	0.059	
>10	0.287	0.357		0.047	0.072	
<b>Histologic subtype</b>			<0.001			0.009
Liposarcoma	0.119	0.162		0.037	0.068	
Leiomyosarcoma	0.238	0.331		0.037	0.060	
Fibromyxosarcoma	0.120	0.156		0.045	0.075	
MFH	0.250	0.318		0.065	0.095	
Hemangiosarcoma	0.525	0.679		0.045	0.045	
MPNST	0.377	0.446		0.038	0.046	
Synovial sarcoma	0.196	0.285		0.025	0.034	
Rhabdomyosarcoma	0.379	0.457		0.032	0.065	
Undifferentiated sarcoma	0.375	0.409		0.035	0.035	
Other	0.259	0.323		0.054	0.078	
<b>Histologic grade</b>			<0.001			0.281
I	0.040	0.064		0.032	0.068	
II	0.100	0.154		0.028	0.056	
III	0.306	0.378		0.054	0.072	
IV	0.316	0.398		0.051	0.071	
<b>SEER stage</b>			<0.001			0.229
Localized	0.130	0.173		0.041	0.069	
Regional	0.279	0.371		0.048	0.071	
Distant	0.659	0.757		0.042	0.046	

**Abbreviations:** Others, American Indian/Alaska Native/Asian/Pacific Islander; MFH, malignant fibrous histiocytoma; MPNST, malignant peripheral nerve sheath tumor; SEER, Surveillance, Epidemiology, and End Results.



**Figure 2** Internal calibration curves. (A) 3-year and (B) 5-year OS nomogram calibration curves; (C) 3-year and (D) 5-year STS CSS nomogram calibration curves. The 45-degree line represents a perfect match between the nomogram-predicted survival (X-axis) and actual survival (Y-axis). The perpendicular line represents 95% confidence intervals of actual survival.

the validation cohort, similar results were obtained in assessment of OS and CSS (Figure 4C and D).

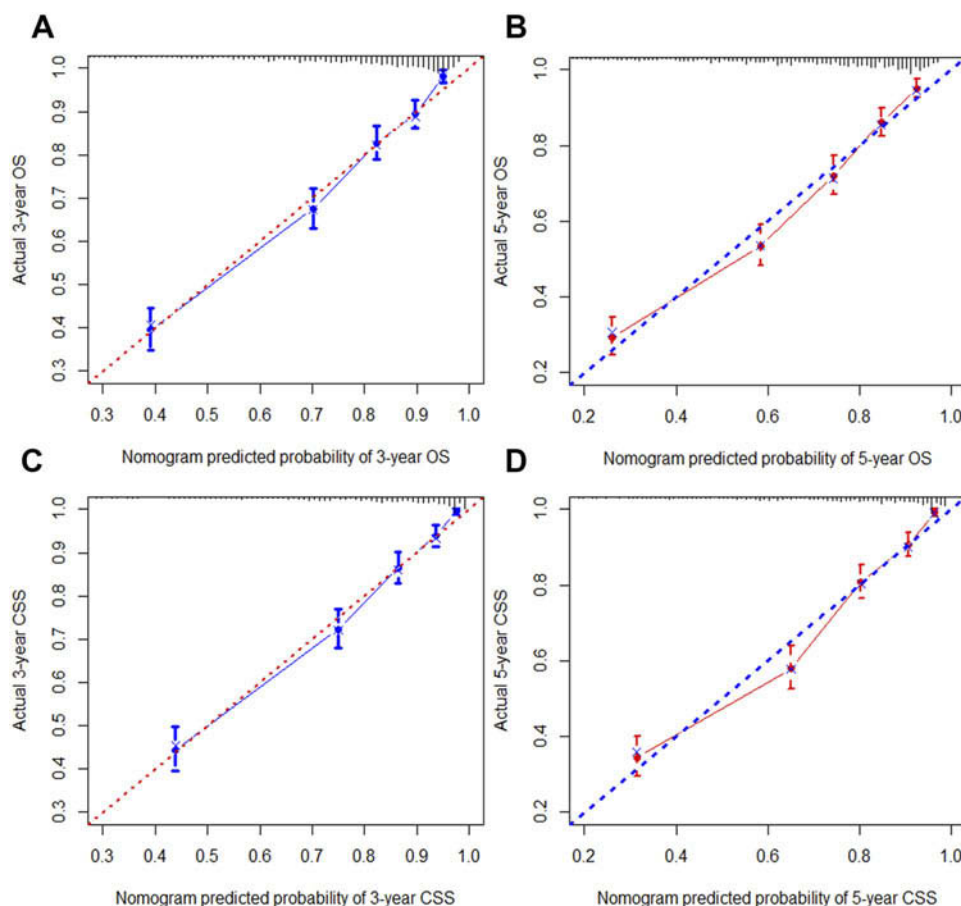
## Discussion

In view of the rarity and heterogeneity of STS, evaluating prognosis has been challenging. To date, a brief nomogram that can estimate the OS and CSS accurately is still lacking. Herein, using the SEER database, we established and validated the first two prognostic nomograms for predicting the 3- and 5-year OS and CSS of the STS patients who underwent surgery. The nomograms showed excellent predictive performance in both internal and external validation. Furthermore, DCA showed that our nomograms outperformed the AJCC staging system with better clinical applicability. With our easily used nomograms, we can identify patients with different prognosis, thus facilitating individualized treatment and follow-up schedule.

At present, the area under curve (AUC) of the receiver operating characteristic (ROC) curve is often used to

assess the prognostic model. However, the AUC merely represents the sum of accuracy and specificity of a model without considering the follow-up clinical influences of the predictive parameters: For example, the model with higher AUC score usually has high sensitivity, but strictly limited specificity.<sup>16</sup> Decision curve analysis (DCA) is a simple and understandable mathematical model, and can evaluate the clinical applicability of a model. To our knowledge, no nomogram has introduced DCA to evaluate the clinical applicability and benefits. Hence, to avoid defects in the previous nomograms, we used DCA in our analysis, and the results showed that our nomograms had better clinical applicability with more net benefits than the current AJCC stages.

In particular, we assessed CSS using cumulative incidence function, which is robust method for analyzing CSS when competing events exist.<sup>17</sup> And we furthermore built the competing risk nomograms to predict the probability of CSS. In clinical oncology, competing risks arise when



**Figure 3** External calibration curves. (A) 3-year and (B) 5-year OS nomogram calibration curves; (C) 3-year and (D) 5-year STS CSS nomogram calibration curves. The 45-degree line represents a perfect match between the nomogram-predicted survival (X-axis) and actual survival (Y-axis). The perpendicular line represents 95% confidence intervals of actual survival.

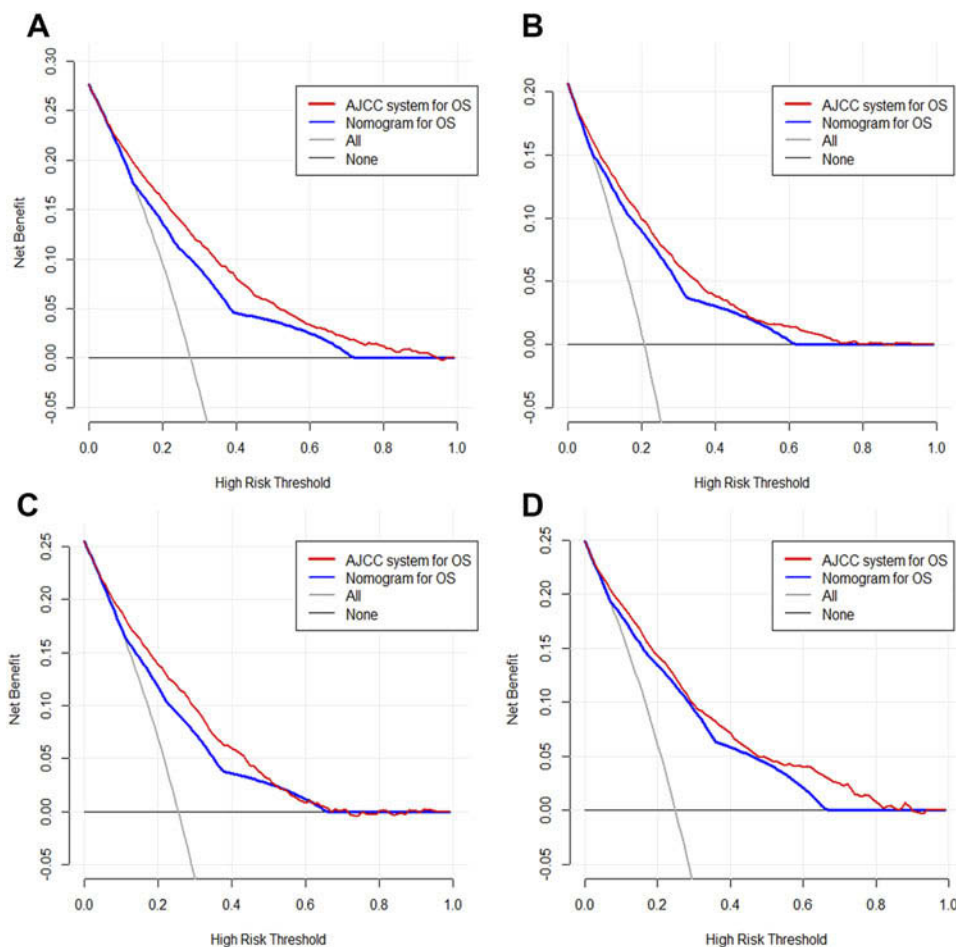
death from other causes precludes the occurrence of CSS.<sup>18</sup> In our study, among the 3,003 deaths in the training cohort, 2,434 (24.9%) deaths resulted from STS, while 569 (5.8%) died secondary to other causes. The 3- and 5-year cumulative incidences of death from STS were 0.258 and 0.325, respectively. Importantly, we observed increasing age had a negative effect on both deaths from STS and other causes. One possible reason for this phenomenon is that older patients more tend to suffer age-related comorbidities or postoperative complications and this would increase with age. These disadvantage conditions were to some extent disqualify them to undergo the same standard of therapy that offered for their younger counterparts. Thus, it is important to consider non-cancer-specific death when estimating survival for STS patients treated with surgery, especially for patients of older ages.

Several clinicopathologic characteristics were identified to be independent prognostic factors for OS in STS patients who underwent surgery, including age, sex, tumor

grade, and TNM classifications, which was in line with the previous studies.<sup>19–21</sup> In the training cohort, the HR of OS increased with age, patients older than 75 years had the worst survival among the STS patients. Sex is an important variable associated with different prognosis in cancers patients.<sup>20</sup> In our analysis, the male STS patients experienced a worse survival compared to female patients. In addition, histological grade was imbedded to our nomogram for its high predictive value in our analysis. Histological differentiation could reflect the biological behaviors of malignant tumor, which had been used to predict survival in several models regarding STS.<sup>22,23</sup>

In recent years, researchers have paid more and more attention on the impact of socioeconomic status on cancer.<sup>24,25</sup> Hence, the socioeconomic status was investigated in our analysis, which was not mentioned in all the previous nomograms for STS patients. It is the first time shown that insurance was an independent prognostic factor and was incorporated to newly prognostic nomogram





**Figure 4** Decision curve analysis of the nomograms and AJCC staging system in terms of OS (A) and CSS (B) in the training cohort and OS (C) and CSS (D) in the validation cohort. The nomograms obtain more net benefits than the AJCC staging system with a wider range of threshold probabilities.

for STS patients with surgery. Uninsured status would lead to decreased diagnosis rates and increased conservative treatment for cancers,<sup>26</sup> thus undermine patients' prognosis. Nowadays, the treatment for STS has become multidisciplinary and expensive. Conceivably, uninsured patients have fragile financial networks, which ultimately may hinder access to adequate management at superior hospitals, and the timely treatment of recurrent cancer. As a potential marker of socioeconomic status,<sup>27</sup> married status was an independent prognostic factor for both OS and CSS, which accorded with our previous study.<sup>28</sup> The married patients tend to enjoy better mental status and strong social support networks, including psychological support and financial resources,<sup>29</sup> so that they could easily get access to the superior quality of the medical treatment and nursing service, which might contribute to their survival advantages. Therefore, we suggested the incorporation of socioeconomic status into prognosis evaluation systems for STS patients.

Nomograms display a wide application prospect in modern medical decision-making. They provide graphical depiction of statistical model that combines multiple parameters to calculate the probability of certain event.<sup>30–33</sup> Accumulating evidence has documented that the nomogram shows higher prediction accuracy than the current AJCC staging system in multiple cancers, and thus it has been accepted as an alternative or even a novel staging system.<sup>34–36</sup> For example, two T3N0M0 STS patients: case A) a 55-year-old married female patient, with grade IV fibromyxosarcoma, who had insurance, and case B) a 65-year-old unmarried man patient diagnosed with grade III hemangiosarcoma, who had no insurance. The survival outcomes of these patients were identical if we used the AJCC staging system. In contrast, according to our nomograms, the 5-year predicted OS for the case A and B were 92% and 58%, respectively. Moreover, the 5-year predicted CSS of the case A and B were 90% and 41%, respectively. These results well elucidated the flaws of the AJCC staging system in forecasting individual prognosis.

Inevitably, several potential limitations in our study should be mentioned. First, as a retrospective study, it has several inherent biases, such as selection bias and missing data, which might lead to inaccurate conclusions. Therefore, to further confirm the results, large prospective cohort or clinical trials may be required. Second, several prognostic factors, such as comorbidity,<sup>37</sup> vascular invasion,<sup>38</sup> surgical margin status,<sup>39,40</sup> chemotherapy or other types of therapy, were not accessible in the SEER database, so we did not incorporate factors into our nomograms. For the same reason, we could not develop the nomogram for predicting disease-free survival and loco-regional control. Third, marital or insurance status might change after registering to the database or during the therapeutic process. Fourth, the SEER database only captures population data from certain states or regions and may, therefore, have some additional limitations in this respect compared with other national datasets. Nevertheless, this population was racially diverse and included patients from almost thousands of hospitals, our nomograms remained suitable for universal application. Finally, we used the same retrospective dataset to construct and validate the nomograms. To further improve the accuracy of our nomograms, prospective validation is warranted, or at least, external validation with independent study cohort.

## Conclusion

In conclusion, we developed and validated the nomograms that estimated 3- and 5-year OS and CSS for STS patients based on a large population-based study cohort. These nomograms demonstrated more accurate and practical performance than the AJCC staging system. Our nomograms could contribute to more individualized and precise management strategies for STS patient.

## Disclosure

The authors report no conflicts of interest in this work.

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