Prognosis and conditional nomogram of cervical spine fracture in patients with severe spinal cord injury: a multicenter retrospective study

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Introduction: Cervical spine fractures with severe spinal cord injury (SCI) are common following cervical spine trauma and are associated with a high mortality rate. Understanding the mortality patterns of patients with cervical spine fractures and severe SCI can offer valuable evidence to surgeons and family members who are required to make critical healthcare decisions. The authors aimed to evaluate the instantaneous death risk and conditional survival (CS) of such patients and developed conditional nomograms to account for different periods of survivors and predict the survival rates.
Methods: Their instantaneous death risks were calculated using the hazard function, and the Kaplan–Meier method was used to evaluate the survival rates. Cox regression was used to choose the variables for the construction of the nomograms. The area under the receiver operating characteristic curve and calibration plots were used to validate the performance of the nomograms.
Results: The authors finally included 450 patients with cervical spine fractures and severe SCI using propensity score matching. The instantaneous death risk was the highest during the first 12 months after injury. Surgical treatment can help decrease the instantaneous death risk quickly, especially in early-term surgery. The 5-year CS increased constantly from 73.3% at baseline to 88.0% after 2 years of survival. Conditional nomograms were constructed at baseline and in those who survived for 6 and 12 months. The area under the receiver operating characteristic curve and calibration curves indicated that the nomograms had a good performance.
Conclusion: Their results improve our understanding of the instantaneous death risk of patients in different periods following injury. CS demonstrated the exact survival rate among medium-term and long-term survivors. Conditional nomograms are suitable for different survival periods in predicting the probability of survival. Conditional nomograms help in understanding the prognosis and improve the shared decision-making approaches.

Keywords: cervical spine fracture, conditional nomogram, conditional survival, instantaneous death risk, severe spinal cord injury

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HIGHLIGHTS

- We provided the instantaneous death risk data of these populations, which adds to our knowledge regarding the instantaneous death risk faced by patients in different time periods and has not been reported previously.
- We showed the conditional survival rates of these patients, which helps us understand the exact survival rate among medium-term and long-term survivors.
- We developed conditional nomograms suitable for different survival periods to accurately predict the survival rates and to fulfill our drive toward personalized medicine.
- We created nomograms with favorable discrimination and predictive abilities with which to predict survival rates.

Introduction

Cervical spine fractures are very common, and their incidence is rising[1]. The incidence of cervical spine fractures is ∼0.29 per 1000 person-years in the U.S.[2]. The common causes of cervical spine fractures include motor vehicle accidents, falls, violence, and sports activities[3,4]. Spinal cord injury (SCI) is the most

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common complication following cervical spine fractures. The annual incidence of SCI is ~0.93 million globally[5]. The prevalence of SCI in patients with cervical spine fractures is ~10–51%[2,6–8]. Cervical spine fractures with severe SCI can lead to high mortality, severe disability, central neuropathic pain, and a large socioeconomic burden[9–12].

The primary management approach for cervical spine fractures with severe SCI is early surgical decompression, which can significantly reduce further neurologic injury[13]. Although patients with cervical spine fractures and severe SCI will surely benefit from surgical management[14], surgeries may be delayed or not performed due to several reasons[15]. One important reason is that patients' families may not consent to surgical treatment when other management options are available[16]. Therefore, knowing the precise instantaneous death risk and mortality rates in cervical spine fractures with severe SCI can offer valuable knowledge and evidence to surgeons and family members in making critical healthcare decisions.

Unlike traditional survival analyses, we aimed to use a hazard function to calculate the instantaneous death risk in such patients. Additionally, the mortality risk in these patients is relatively high in the first several months following injury and decreases over time. Therefore, the survival rates calculated at baseline may not be appropriate during the follow-up. Conditional survival (CS) only includes patients who have already survived for a certain period and is a more appropriate parameter in such situations[17,18]. However, CS is commonly used in cancer research[19], and to the best of our knowledge, we are the first to propose the use of this concept in the interpretation of survival rates in patients with cervical spine fractures and severe SCI.

Nomograms are commonly used as prognostic devices to calculate the probability of a clinical event in medicine and cancer[20]. However, similar to traditional survival analyses, nomograms based on baseline parameters cannot accurately predict the survival rates of medium-term or long-term survivors.

Therefore, in this study, the hazard function was used to calculate the instantaneous death risk of such patients, and CS was used to estimate the precise survival rates of survivors during fixed periods. We also constructed a series of nomograms to predict the prognoses of these patients. In this study, we aimed to determine the instantaneous death risk and CS of patients with cervical fractures and severe SCI. Additionally, we developed conditional nomograms to account for the survival of different durations to accurately predict the survival rate and promote personalized medicine.

Methods

The study and the informed consent protocol were approved by the ethics committee of Xijing Hospital of Air Force Medical University (KY20212199-F-1). Our results are reported in line with STROCSS (strengthening the reporting of cohort, cross-sectional and case–control studies in surgery) 2021 criteria[21], Supplemental Digital Content 1, http://links.lww.com/JS9/A211.

Patient data were obtained from Xijing Hospital, Xi'an Honghui Hospital, Tangdu Hospital, The Second Affiliated Hospital of Xi'an Jiaotong University, and Wenzhou Medical University Second Affiliated Hospital. These are locally affiliated tertiary care centers with extensive experience in treating patients with cervical fractures and severe SCI. Patients admitted to these

hospitals with cervical fractures and severe SCI between 1 January 2012 and 30 May 2019, were included.

The inclusion criteria were the following: cervical fractures (confirmed using imaging) and severe SCI [American Spinal Injury Association impairment scale (ASIA) grade A or B][22]. ASIA grade A is defined as the absence of all motor and sensory functions, and ASIA grade B is defined as patients having some sensory function but no motor function.

The following were the exclusion criteria: serious infections, blood dyscrasias, tumors, or congenital spinal deformities; serious cardiopulmonary diseases; death prior to hospital admission; ankylosing spondylitis, diffuse idiopathic skeletal hyperostosis, or other chronic spondylitis disorders; ASIA grades C, D, or E (ASIA grade C is defined as patients whose motor function is preserved below the neurological level, and more than half of key muscles below the neurological level have a muscle grade less than 3, while ASIA grade D is defined as patients whose motor function is preserved below the neurological level, and at least half of key muscles below the neurological level have a muscle grade of 3 or more. Patients with ASIA grade E may have normal motor and sensory examinations, but still may have abnormal reflexes or other neurologic phenomena); only thoracic or lumbar injuries; and brain injury.

The reason for the first two exclusion criteria is that these comorbidities may adversely affect the prognosis, which may result in an underestimation of the survival rate. Similarly, including patients who died before reaching the hospital can also result in an underestimation of the survival rate since most patients were likely directly killed by serious traffic accidents. Furthermore, the mortality in patients with cervical fractures and ankylosing spondylitis or diffuse idiopathic skeletal hyperostosis tends to be much higher than that in patients without these conditions[23]. Therefore, including such patients may also result in an underestimation of the general survival rate. Patients with brain injury were also excluded because brain injury may interfere with ASIA grading.

We collected data such as demographic characteristics, comorbidities, cervical spine fracture levels, dislocation status (yes or no), injury mechanism, ASIA grade, the surgery type and timing, and common complications. To avoid any possible bias, the baseline characteristics were compared between patients who were included and those who were lost to follow-up. There was no significant difference between the groups. The included patients were followed up from admission until death or 1 June 2022, whichever was later. Data regarding death were collected via phone calls, short messages, or household registration agencies in government departments.

Propensity score matching with 1 : 1 matching was used to form two groups of patients, which could reduce the bias between groups[24]. The propensity score was calculated using a logistic regression model with the following variables: age, injury factors, fracture level, comorbidities, surgical treatment, operation timing, and complications. The matching was performed using the nearest neighbor matching method with a caliper width of 0.20.

According to the ASIA scale, we conducted neurological examinations at the time of admission to evaluate the degree of SCI. We divided the fracture levels into two subgroups: upper cervical spine fractures (C1–C4) and lower cervical spine fractures (C5–C7). Injury mechanisms were divided into low-energy injuries (due to a fall on the ground or sports activities) and high-energy injuries (due to motor vehicle accidents, fall from height,

or violence). Experienced spine surgeons decide on the surgery type through discussion and then perform the surgeries. The timing of surgery was defined as the duration between the injury and surgery. We divided the timing of surgery into early (<3 days), medium (3–7 days), and late (>7 days) surgery durations.

Statistical analyses

The instantaneous death risk was calculated using a hazard function curve with a fixed bandwidth kernel approach that incorporated boundary kernels[25,26]. The Kaplan–Meier (KM) method was used to evaluate the survival rates, and the log-rank test was used to test the statistical differences between subgroups. Cox regression models were used to determine the risk factors for mortality. Variables with P values less than 0.05 in the univariate Cox analysis were included in the multivariate Cox analysis. The multivariable Cox regression was fitted using stepwise backward selection based on Akaike's Information Criterion[27]. Finally, factors with prognostic significance in the multivariate Cox regression analysis were used to build nomograms, which were developed using the rms package in R v4.1.2 (R Foundation for Statistical Computing, Vienna, Austria)[28].

The 5-year CS was defined as the probability of survival for 5 years from the day that the patients had already survived for a period of time[29]. For example, the 5-year CS at 1 year refers to the survival rate for 5 years in patients who had already survived for 1 year. The details of the calculations have been provided previously[30]. Restricted cubic splines were used to find the relationship between the probability of death and age and to identify the cutoff limit for age.

The area under the receiver operating characteristic curve (AUC) and the area under the time-dependent receiver operating characteristic curve (time-dependent AUC) was calculated to assess discriminative ability. Generally, AUC greater than 0.7 indicated a reasonable estimation. Calibration plots were calculated to assess the calibrating ability using the bootstrapping method (1000 resampling bootstrap)[31]. Agreement between observed and predicted outcomes was evaluated using calibration plots, which incorporated grouped KM estimates and the continuous hazard regression function[31].

Statistical analyses were conducted using STATA v14.2 (Stata Corp., College Station, Texas, USA), SPSS v22.0 (IBM Corporation, Armonk, New York, USA), and R v4.1.2 (R Foundation for Statistical Computing). Continuous variables are presented as mean ± SD or median [interquartile range (IQR)] and were compared using the independent sample t test or the Mann–Whitney U test, as appropriate. Categorical variables are presented as frequencies (%) and compared using the χ^2 or Fisher's exact tests. The statistical significance was set at P less than 0.05.

Results

Finally, we included 450 patients for further analysis after using propensity score matching. The overall mean age of the patients was 46.3 ± 15.5 and 45.6 ± 15.3 years in patients with ASIA grade A and grade B, respectively. Nearly 80% of the patients experienced high-energy injuries that resulted in cervical spine fractures (Table 1). Approximately 40% of patients had upper cervical spine (C1–C4) fractures. More than 80% of the patients

Table 1

Baseline characteristics after propensity score matching.

Demographics	ASIA A (n = 225)	ASIA B (n = 225)	P
Age, years			
Mean (SD)	46.3 (15.5)	45.6 (15.3)	0.657
Median (IQR)	46 (33–55)	45 (35.5–60)	0.883
Sex			0.886
Male	197 (87.6)	198 (88.0)	
Female	28 (12.4)	27 (12.0)	
Dislocation	86 (38.2)	79 (35.1)	0.493
Injury factors			0.107
High-energy injury	192 (85.3)	179 (79.6)	
Low-energy injury	33 (14.7)	46 (20.4)	
Fracture level			0.126
Upper cervical spine (C1–C4)	86 (38.2)	102 (45.3)	
Lower cervical spine (C5–C7)	139 (61.8)	123 (54.7)	
Comorbidity			
Chest injury	35 (15.6)	49 (21.8)	0.090
Fractures in other parts	37 (16.4)	23 (10.2)	0.052
Hypertension	8 (3.6)	9 (4.0)	0.805
Diabetes	7 (3.1)	8 (3.6)	0.793
Surgical treatment			0.209
Yes	200 (88.9)	191 (84.9)	
No	25 (11.1)	34 (15.1)	
Operation timing			0.357
Nonsurgery	25 (11.1)	34 (15.1)	
Early term	60 (26.7)	57 (25.3)	
Medium term	101 (44.9)	87 (38.7)	
Later term	39 (17.3)	47 (20.9)	
Complications			
Pneumonia	55 (24.4)	46 (20.4)	0.309
Respiratory failure	9 (4.0)	13 (5.8)	0.382
Deep veinous thrombosis	1 (0.4)	2 (0.9)	0.562
Decubitus	3 (1.3)	8 (3.6)	0.127
Urinary tract infection	10 (4.4)	6 (2.7)	0.309

ASIA, American Spinal Injury Association impairment scale; IQR, interquartile range.

underwent surgeries, and pneumonia was the commonest complication.

Instantaneous death risk and survival curve

The instantaneous death risk was the highest at the time of injury and rapidly decreased in the first 12 months after injury (Fig. 1A–G). In the first 12 months after the injury, the instantaneous death risk fluctuated within a relatively low-risk range. We also found that surgical treatments, especially early-term surgery, decreased the instantaneous death risk more quickly than nonsurgical treatments (Fig. 1C, E). Additionally, we observed that the instantaneous death risk increased significantly when patients developed pneumonia or respiratory failure (Fig. 1D, G).

We found that patients with ASIA grade A and high-energy injuries were more likely to die (Fig. 1I, K). Additionally, the survival rates were improved by surgeries, especially with early-term surgical treatment (Fig. 1J). However, hypertension, pneumonia, and respiratory failure significantly decreased the survival of the patients with severe SCI (Fig. 1L–N).
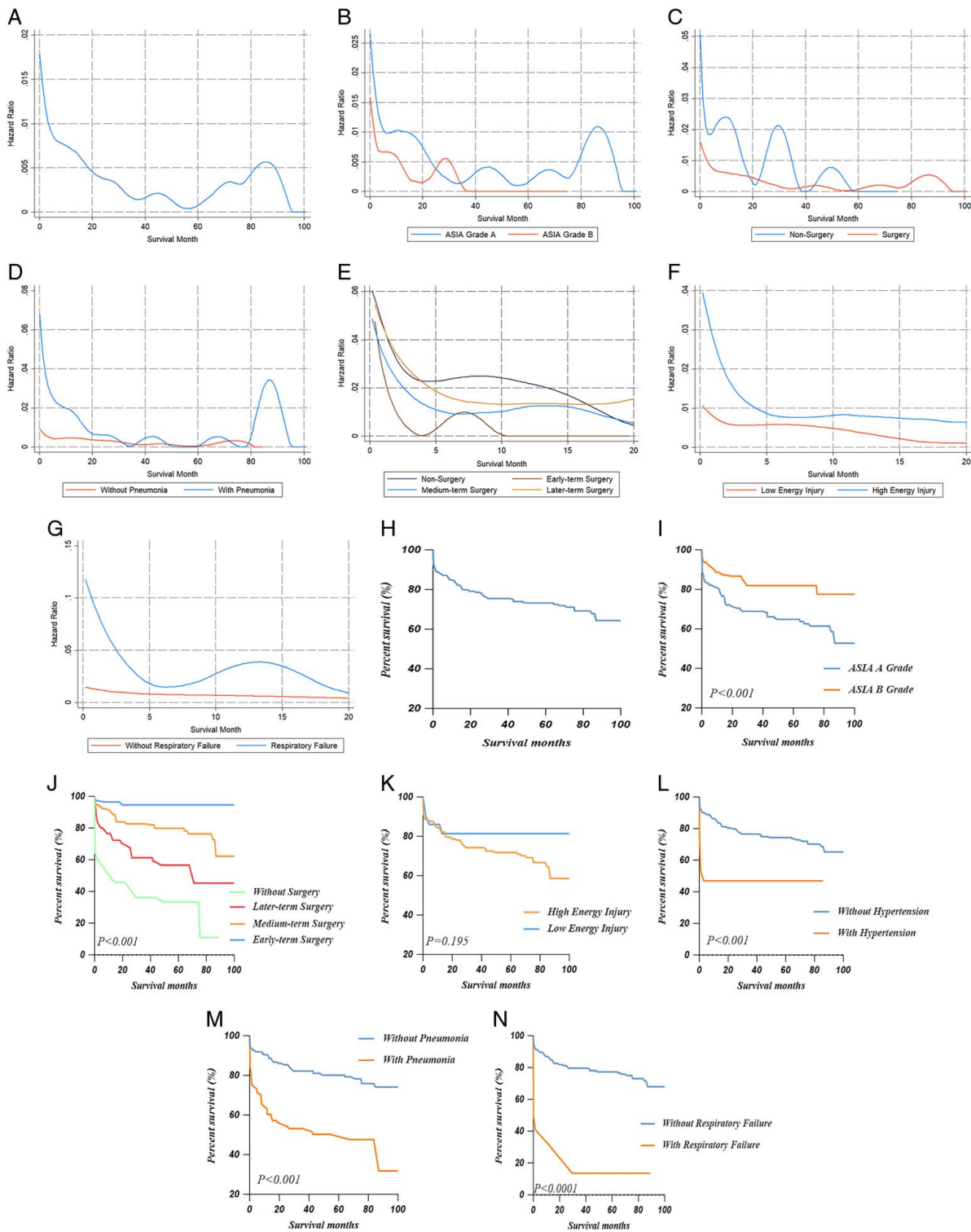
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Figure 1. Hazard function curve for instantaneous death risk in cervical spine fracture patients with severe SCI (A) and stratified by ASIA grade (B), surgery (C), pneumonia (D), surgery timing (E), injury energy (F) and respiratory failure (G). Kaplan–Meier survival curves illustrating the overall survival (H) and stratified by ASIA grade (I), surgery timing (J), injury energy (K), hypertension (L), pneumonia (M), and respiratory failure (N). ASIA, American Spinal Injury Association impairment scale; SCI, spinal cord injury.

We found that the optimal cutoff limit for age was 45 years (Fig. 2). Therefore, patients under 45 years of age had a low risk of death, while those older than 45 years had a high risk of death. We further conducted prognosis analysis to identify the prognoses in patients of different ages (Supplementary Figures 1, Supplemental Digital Content 2, http://links.lww.com/JS9/A212 and 2, Supplemental Digital Content 3, http://links.lww.com/JS9/A213). The prognosis was found to be worse in patients older than 45 years of age ($P < 0.001$).
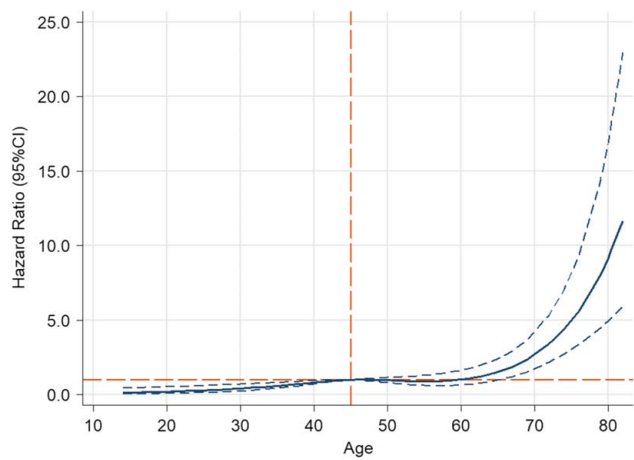
Figure 2. Cubic spline models showing the association between age and mortality risk. The long orange dashed transverse line represents the hazard ratio of 1. The long dashed orange vertical line represents the age of 45. The solid blue line and the long dashed blue line represent the estimated hazard ratio and its 95% CI.

5-year CS in patients with cervical spine fracture and severe SCI

We noted that the 5-year CS increased constantly from 73.3% at baseline to 88.0% after 2 years of survival (Table 2). We also found that the 5-year CS in patients with ASIA grade A increased from 64.9% at baseline to 87.1% after 2 years of survival, whereas that in patients with high-energy injuries increased from 71.8% at baseline to 85.4% after 2 years of survival. Patients who had respiratory insufficiency had the lowest 5-year survival rate at baseline (13.6%); however, their survival rate significantly increased after 2 years of survival (50.0%). Similarly, patients with pneumonia had a significantly low 5-year survival rate (50.4%); however, their 5-year survival rate gradually increased after surviving for a certain period. Additionally, the 5-year CS in different age groups was also tested. We found that the 5-year survival rate in patients under 45 years of age was relatively high

(Supplementary Table 1, Supplemental Digital Content 4, http://links.lww.com/JS9/A214). However, the 5-year survival rates increased from 54.4 to 74.8% in patients older than 60 years after 2 years of survival.

Cox regression analysis

At baseline, we found that age, ASIA grade A, nonsurgical treatment, pneumonia, and respiratory failure were risk factors for death (Table 3). However, in patients who had already survived for 12 months, we found that age, nonsurgical treatment, ASIA grade A, respiratory failure, and decubitus were risk factors for death (Table 3). Only early surgical treatment was a constant predictor of survival at baseline [hazard ratio (HR): 0.08, 95% CI: 0.03–0.20, $P < 0.001$], 6 months (HR: 0.06, 95% CI: 0.02–0.25, $P < 0.001$), and 12 months (HR: 0.07, 95% CI: 0.01–0.39, $P = 0.002$).

Conditional nomogram construction and validation

We constructed nomograms at baseline (Fig. 3A) and in 6-month (Fig. 3D) and 12-month survivors (Fig. 3G) according to the risk factors. For the first injury and follow-up, we first chose a suitable nomogram and then added the individual scores to obtain a total score. Finally, we used the total score to predict an individual's 1-year, 3-year, and 5-year survival probabilities.

We further investigated the performance of these nomograms. The AUC in the training cohort was 0.856 at baseline (Fig. 3B), 0.857 in 6-month survivors (Fig. 3E), and 0.801 in 12-month survivors (Fig. 3H). More importantly, the time-dependent AUC in survivors of various durations remained greater than 0.8 in the prediction of survival for 5 years (Fig. 3C, F, I).

The calibration curves of the nomograms that were applied to the training and validation cohorts are also shown (Fig. 4). The results revealed that the nomograms had a good agreement in predicting the survival probability between the predicted survival rates and observed survival rates in both the training and validation cohorts.

Table 2

Five-year conditional survival rates.

Variables	Conditional 5-year relative survival (%)				
	5-Year relative survival at baseline (%)	At 3 months (%)	At 6 months (%)	At 1 year (%)	At 2 years (%)
Total	73.3 ± 2.2	82.5 ± 2.1	83.2 ± 2.1	84.5 ± 2.3	88.0 ± 2.7
ASIA grade					
A grade	64.9 ± 3.4	76.0 ± 3.5	76.3 ± 3.7	77.1 ± 3.9	87.1 ± 3.6
B grade	82.1 ± 2.7	87.5 ± 2.4	88.8 ± 2.3	87.5 ± 3.9	89.5 ± 3.9
Injury mechanism					
High-energy injury	71.8 ± 2.5	81.0 ± 2.3	81.2 ± 2.4	82.6 ± 2.7	85.4 ± 3.3
Low-energy injury	81.5 ± 4.5	90.6 ± 3.7	94.6 ± 3.0	94.6 ± 3.0	100
Surgery					
Yes	79.8 ± 2.2	85.7 ± 2.0	85.8 ± 2.2	86.4 ± 2.3	92.4 ± 2.1
No	31.5 ± 6.4	51.6 ± 9.0	51.6 ± 9.0	64.0 ± 9.9	68.8 ± 10.1
Pneumonia					
Yes	50.4 ± 5.1	66.9 ± 5.6	70.6 ± 5.6	75.3 ± 6.5	84.8 ± 6.3
No	80.2 ± 2.3	86.4 ± 2.1	87.2 ± 2.1	87.8 ± 2.2	88.9 ± 2.9
Respiratory insufficiency					
Yes	13.6 ± 7.3	33.3 ± 15.7	33.3 ± 15.7	42.9 ± 18.7	50.0 ± 20.4
No	77.4 ± 2.1	84.7 ± 2.0	85.5 ± 2.0	86.4 ± 2.3	89.9 ± 2.6

ASIA, American Spinal Injury Association impairment scale

Table 3

Univariable and multivariable Cox regression results of the risk factors of mortality in baseline, ≥6-month and 12-month survivors.

	Baseline survivors				≥ 6 months survivors				≥ 12 months survivors			
	Hazard ratio (95% CI)	P	Hazard ratio (95% CI)	P	Hazard ratio (95% CI)	P	Hazard ratio (95% CI)	P	Hazard ratio (95% CI)	P	Hazard ratio (95% CI)	P
Covariables	Univariable analysis		Multivariable analysis		Univariable analysis		Multivariable analysis		Univariable analysis		Multivariable analysis	
Age	1.05 (1.04–1.06)	<0.001	1.04 (1.02–1.05)	<0.001	1.03 (1.01–1.05)	0.002	1.02 (1.00–1.04)	0.045	1.04 (1.02–1.06)	0.001	1.05 (1.02–1.07)	<0.001
Sex												
Male	Ref	Ref	–	–	Ref	Ref	–	–	Ref	Ref	–	–
Female	0.97 (0.54–1.72)	0.908	–	–	0.76 (0.30–1.90)	0.556	–	–	0.76 (0.27–2.13)	0.607	–	–
Cervical fracture site												
C1–C4	Ref	Ref	–	–	Ref	Ref	–	–	Ref	Ref	–	–
C5–C7	0.93 (0.65–1.35)	0.709	–	–	0.73 (0.43–1.24)	0.246	–	–	1.62 (0.88–3.00)	0.124	–	–
Dislocation	0.79 (0.54–1.13)	0.198	–	–	0.74 (0.44–1.23)	0.240	–	–	0.90 (0.50–1.62)	0.719	–	–
ASIA grade												
A grade	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
B grade	0.42 (0.28–0.62)	0.001	0.29 (0.19–0.43)	<0.001	0.43 (0.25–0.74)	0.002	0.31 (0.17–0.56)	<0.001	0.30 (0.15–0.57)	<0.001	0.20 (0.09–0.44)	<0.001
Injury mechanism												
High-energy injury	Ref	Ref	–	–	Ref	Ref	Ref	Ref	Ref	Ref		
Low-energy injury	0.59 (0.34–1.04)	0.068	–	–	0.22 (0.07–0.70)	0.011	0.28 (0.08–0.94)	0.039	0.27 (0.10–0.90)	0.033	0.48 (0.14–1.64)	0.241
Comorbidity												
Hypertension	3.42 (1.73–6.77)	<0.001	1.66 (0.79–3.49)	0.183	20.73 (0.01–82694.02)	0.586	–	–	0.05 (0.00–574.32)	0.527	–	–
Diabetes	0.72 (0.23–2.27)	0.575	–	–	1.46 (0.46–4.66)	0.527	–	–	0.05 (0.00–54.21)	0.395	–	–
Chest injury	2.25 (1.26–4.00)	0.006	1.53 (0.80–2.92)	0.201	1.54 (0.78–3.05)	0.211	–	–	0.86 (0.43–1.73)	0.670	–	–
Fractures in other parts	4.89 (1.80–13.26)	0.002	2.49 (0.87–7.18)	0.091	26.17 (1.24–552.81)	0.036	–	0.956	0.04 (0.00–1.18)	0.062	–	–
Complications												
Pneumonia	3.52 (2.44–5.07)	<0.001	2.39 (1.63–3.52)	<0.001	3.18 (1.89–5.35)	<0.001	1.94 (1.12–3.36)	0.018	2.52 (1.37–4.63)	0.003	1.93 (0.95–3.92)	0.069
Respiratory failure	8.14 (4.95–13.38)	<0.001	3.79 (1.93–7.47)	<0.001	5.94 (2.54–13.88)	<0.001	3.09 (1.04–9.13)	0.042	5.47 (1.95–15.35)	0.001	68.98 (15.66–303.77)	0.006
Deep veinous thrombosis	1.72 (0.24–12.29)	0.591	–	–	–	0.715	–	–	–	0.750	–	–
Decubitus	1.08 (0.34–3.40)	0.899	–	–	2.40 (0.74–7.74)	0.144	–	–	3.54 (1.07–11.64)	0.038	5.34 (1.30–21.89)	0.020
Urinary tract infection	1.25 (0.55–2.85)	0.594	–	–	1.94 (0.77–4.88)	0.159	–	–	2.49 (0.98–6.36)	0.056	–	–
Operation timing												
Nonsurgery	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Early term	0.04 (0.17–0.10)	<0.001	0.08 (0.03–0.20)	<0.001	0.04 (0.01–0.14)	<0.001	0.06 (0.02–0.25)	<0.001	0.05 ((0.01–0.21)	<0.001	0.07 (0.01–0.39)	0.002
Medium term	0.21 (0.13–0.32)	<0.001	0.34 (0.19–0.61)	<0.001	0.29 (0.15–0.54)	<0.001	0.40 (0.18–0.91)	0.028	0.47 (0.21–1.05)	0.065	0.60 (0.20–1.80)	0.362
Later term	0.48 (0.30–0.76)	0.056	0.70 (0.39–1.26)	0.231	0.61 (0.30–1.22)	0.160	1.01 (0.42–2.43)	0.975	0.95 (0.40–2.28)	0.908	1.65 (0.51–5.30)	0.401

ASIA, American Spinal Injury Association impairment scale; Ref, Reference.
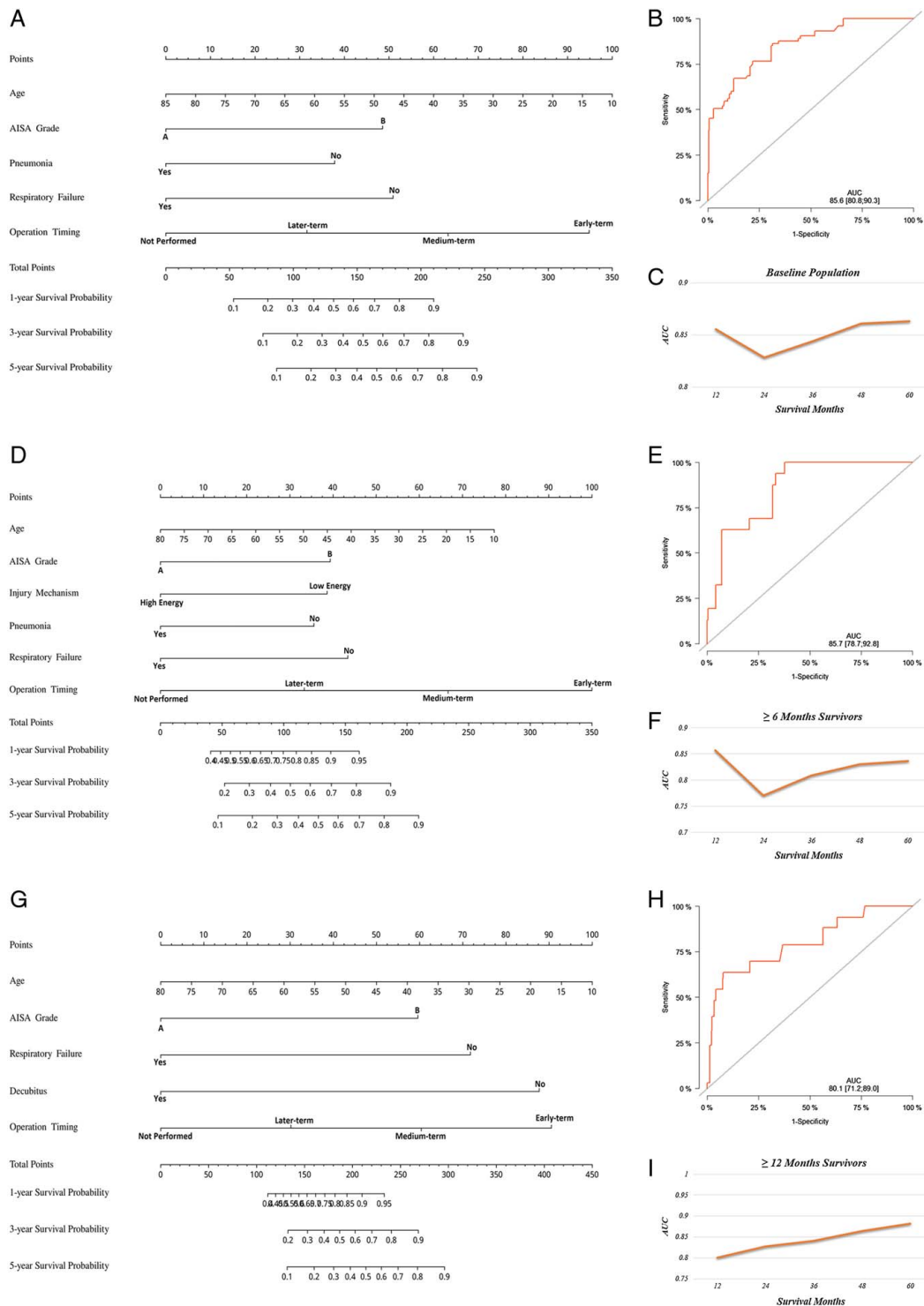
Figure 3. (A) A nomogram to predict 1-year, 3-year, and 5-year survival for baseline patients and validated by AUC (B) and time-dependent AUC (C) in the training cohort. (D) A nomogram to predict 1-year, 3-year, and 5-year survival for 6-month survivors and validated by AUC (E) and time-dependent AUC (F) in the training cohort. (G) A nomogram to predict 1-year, 3-year, and 5-year survival for 12-month survivors and validated by AUC (H) and time-dependent AUC (I) in the training cohort. AUC, area under the receiver operating characteristic curve; time-dependent AUC, under the time-dependent receiver operating characteristic curve.

Discussion

In the present study, we analyzed the detailed survival data of patients with cervical spine fractures and severe SCI. The novelty and strengths of our study include the following: we estimated the instantaneous death risk in these patients for different periods, which adds to the knowledge and has not been reported previously; we estimated the CS rates, which help us understand the precise survival rate in medium-term and long-term survivors; we developed conditional nomograms for different survival periods
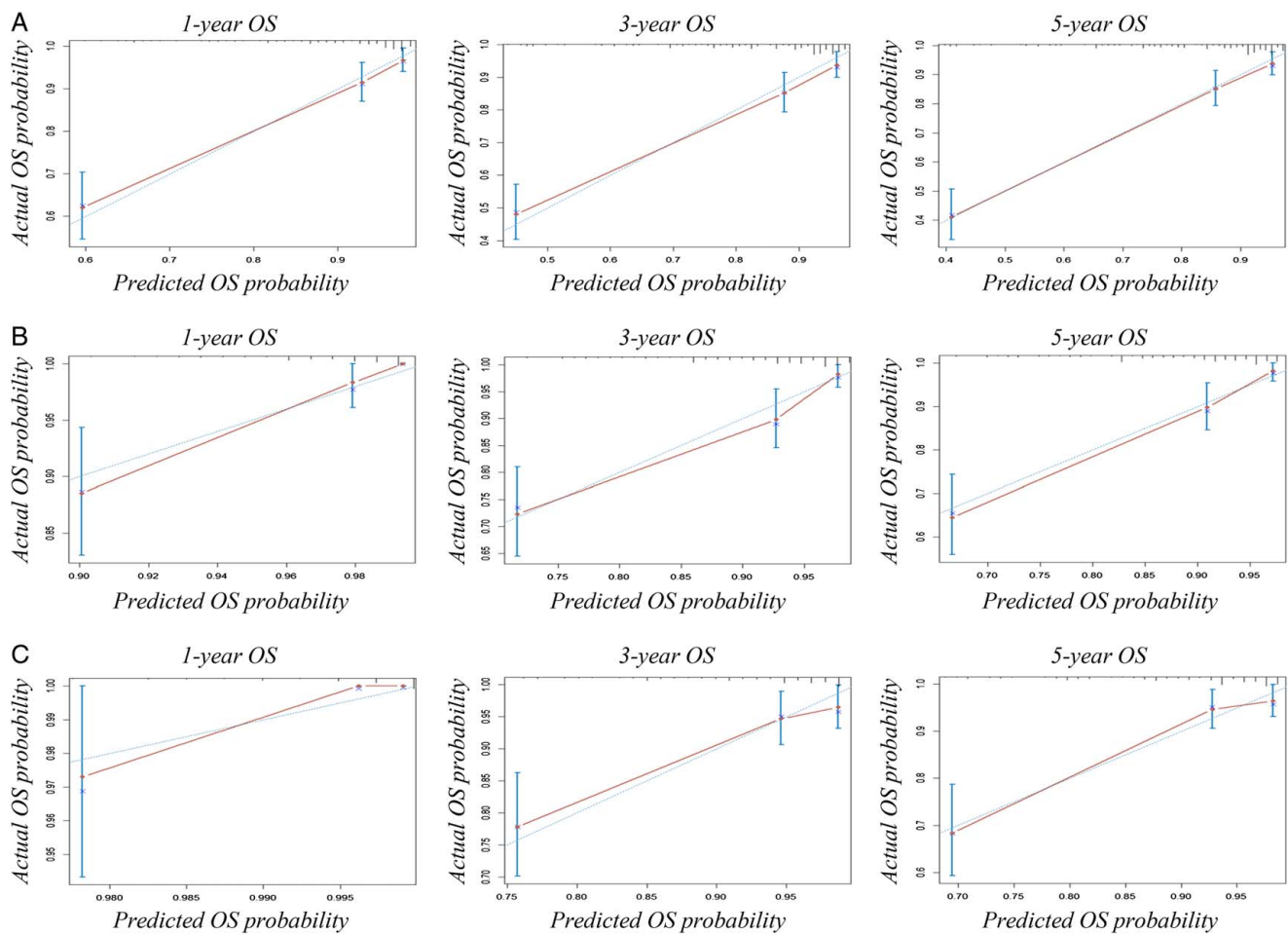
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Figure 4. Calibration curves in the training and validation cohorts. (A) Calibration curves of baseline nomogram to predict 1-year, 3-year, and 5-year survival. (B) Calibration curves of 6-month survivors nomogram to predict 1-year, 3-year, and 5-year survival. (C) Calibration curves of 12-month survivors nomogram to predict 1-year, 3-year, and 5-year survival. OS, overall survival.

to accurately predict the survival rates and push forwards toward personalized medicine strategies; we demonstrated favorable discrimination and predictive abilities of nomograms in predicting survival rates.

Currently, the commonest analysis model for time-to-event data includes KM survival function estimators and life tables[32]. Though these models can provide us with the probability of surviving to time x, we cannot know the instantaneous death risk/rate at time x[33]. Therefore, in the present study, we used the hazard function to estimate the instantaneous death risk/rate at time x. The hazard function depicts the natural interpretation of death[34] and how the risk changes over time in terms of the instantaneous death risk/rate in survivors. Additionally, the hazard function also helps determine the periods with the greatest risk of death[35]. Our findings revealed that the patients had the highest risk of death during the first 12 months following injury, and early surgery could help rapidly decrease this risk. Furthermore, our results also help determine the follow-up in these patients[36,37].

One study reported that the in-hospital mortality rate in this patient population was 38%[38], while another recent study showed that the 1-year mortality rate was 36.5%[16]. In our study, the mortality rate was relatively lower than these reported

rates. One possible explanation may be that previous studies included only older patients. The mortality rate in older patients is significantly higher than that in younger people[39]. However, the cutoff limit for age while dividing the risk of patients has not been clarified. Therefore, we used restricted cubic splines to identify the optimal cutoff limit. Our results revealed that patients older than 45 years of age were at a high risk of death.

Systematic biases are very common in observational studies; however, these are often difficult to overcome[40]. In our present study, we found that surgical treatment was one of the most important factors associated with the prognosis. However, we assumed that this result was affected by selection bias because some patients were unable to undergo surgical treatment. These patients may have greater morbidity, thus resulting in a worse prognosis. Selection bias, which may be attributable to unmeasured variables as well as to a wide range of measured variables, indicates a lack of comparability between study groups. Therefore, we used a multivariate regression model to account for potential confounders in our study. A randomized prospective trial may minimize the effects of selection bias and demonstrate the real benefits of surgical treatment on the prognosis. However, such a trial is difficult to conduct because surgical treatments

cannot be randomized. However, early surgical treatment helps improve the prognosis in general[41], and our results support this point of view.

CS considers the years that a patient has already survived when estimating their survival probability[29,30]. However, this concept is mainly used in the field of cancer. To the best of our knowledge, this is the first study to introduce this concept in the field of severe SCI. Although the traditional survival rate is valuable for patients at baseline, it cannot provide precise survival probability during follow-up. As shown in our study, the 5-year survival rate increased constantly from 73.3% at baseline to 88.0% in 2-year survivors. Notably, in patients with ASIA grade A, the 5-year survival rate increased from 64.9% at baseline to 87.1% after 2 years of survival. Additionally, our results also indicated that the risk factors change with survival time. For example, old age is always a risk factor at baseline as well as at 6 and 12 months, while decubitus is not a risk factor at baseline and in 6-month survivors but is a risk factor in 12-month survivors. On the one hand, knowing the CS and changes in risk factors is critically important for surgeons during follow-up and counseling[42,43]. On the other hand, our results provide new information on how prognoses change over time, which can help doctors and patients observe positive changes in disease mortality.

Previous studies have highlighted that one limitation of nomograms is that they assume that the outcomes remain constant over the survival time[20]. However, the mortality and risk factors vary over the duration of survival[44,45]. Therefore, to remedy this limitation, we developed conditional nomograms to fit different survival periods. A suitable nomogram can be chosen to predict the survival rate of certain survivors more accurately. Additionally, for internal or external validation, the AUC of the nomograms indicated good prediction performance. Furthermore, the calibration plots also demonstrated a good correspondence between the predicted and observed survival rates. Additionally, due to differences in diagnosis, treatments, and prognosis between patients with cervical spine fractures with and without severe SCI, we intend to perform further studies to highlight the differences in the prognosis between these patients.

Our study has some limitations. First, our study was based on retrospective data; therefore, an inherent bias is inevitable. It is important to validate these nomograms in prospective studies. Second, our results were based on data from Chinese patients, and they may not be applicable to other population groups. Therefore, validations in different patient populations are warranted. Third, patients who died before admission were excluded, which may have resulted in an overestimation of the survival rates. Finally, there may be a potential bias due to nonresponses. Previous studies have indicated that nonresponders may be older and have greater morbidities, which might have resulted in selection bias and a lack of representation[46,47]. However, more recent studies have demonstrated that nonresponders did not significantly affect the risk and death estimates[48–51].

Conclusion

We estimated the instantaneous death risk during various periods in patients with cervical spine fractures and severe SCI. We also presented the CS rates in these patients, which improved our understanding of the exact survival rates in medium-term and long-term survivors. Additionally, we constructed conditional nomograms that are suitable for survivors of different periods and can be used as accurate predictive tools for the risk of death. Such clinical tools can help surgeons and patients understand certain prognoses and improve their shared decision-making approaches. Finally, our results support our progress toward personalized medicine.

Ethical approval

The study has been approved by the ethics committee of Xijing Hospital of Fourth Military Medical University (KY20222235-C-1).

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Author contribution

J.H.: conceptualization, methodology, software, data curation, visualization, investigation, and writing – original draft preparation; K.Y.: data curation, methodology, and software; C.W.: software, data curation, visualization, and investigation; Q.-C.T.: software, data curation, and visualization; H.B. and J.W.: software and validation; B.L. and Z.-X.W.: conceptualization, methodology, supervision, and writing – reviewing and editing.

Conflicts of interest disclosure

The authors declare no potential conflicts of interest.

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Data availability statement

Data are available upon reasonable request.

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