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Predicting Surgical Site Infection Risk after Spinal Tuberculosis Surgery: Development and Validation of a Nomogram

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Abstract

Background: The purpose of this study was to predict the surgical site infection risk after spinal tuberculosis surgery based on a nomogram.
Patients and Methods: We collected the clinical data of patients who underwent spinal tuberculosis surgery in our hospital and included all the data in the least absolute shrinkage and selection operator (LASSO) regression analysis. Next, the selected parameters were analyzed using logistic regression. The logistic regression analysis and receiver operating characteristic (ROC) curve analysis were further used to obtain statistically significant parameters. These parameters were then used to construct a nomogram. The C-index, ROC curve, and decision curve analysis (DCA) were used to assess the predictive ability and accuracy of the nomogram, whereas internal verification was used to calculate the C-index by bootstrapping with 1,000 resamples.
Results: A total of 394 patients with spinal tuberculosis surgery were included in the study, of whom 76 patients had surgical site infections whereas 318 patients did not. The predicted risk of surgical site infection in the nomogram ranged between 0.01 and 0.98. Both the value of the C-index of the nomogram (95% confidence interval [CI], 0.62–0.76) and the area under the curve (AUC) were found to be 0.69. The net benefit of the model ranged between 0.01 and 0.99. In contrast, the C-index calculated by the internal verification method of the nomogram was found to be 0.68.
Conclusions: The risk factors predicting surgical site infection after spinal tuberculosis surgery included albumin, lesion segment, operation time, and incision length.

Keywords: nomogram; risk factors; spinal tuberculosis; surgical site infection

Tuberculosis is a specific infectious disease caused by *Mycobacterium tuberculosis*. Because of its increase in annual incidence, it has become a challenge in developing countries [1,2]. Spinal tuberculosis is the most common manifestation of extrapulmonary tuberculosis [3], the symptoms of which include pain, fatigue, fever, night sweats, weight loss, and other symptoms of tuberculosis poisoning [4]. Its clinical treatment generally adopts two measures, antituberculosis treatment and surgery [5,6]. However, there is a risk of surgical site infection after spinal tuberculosis surgery.

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Previous research has also reported surgical site infections after spinal tuberculosis surgery. Liang et al. [7] have shown a superficial infection in one patient among the 30 who underwent spinal tuberculosis surgery. Yang et al. [8] showed that patients with traditional spinal tuberculosis surgery were more likely to get superficial surgical site infections than those who underwent minimally invasive tuberculosis surgery. Zhang et al. [9] reported that despite the surgical treatment of lumbosacral tuberculosis being considered safe and effective, three cases of delayed surgical site healing were still observed. Omran et al. [10] investigated 35 patients with thoracic tuberculosis who underwent posterior extensive circumferential decompressive reconstruction and found three surgical site infection cases. However, the surgical site infection resolved within one month of local debridement [10]. A study by Fukuta et al. [11] showed that surgical site infection after spinal surgery was associated with poor general condition. Also, implant failure after spinal tuberculosis surgery was considered a risk factor for surgical site infection [12]. However, no reports exist in the literature of models that predict risk factors of surgical site infection after spinal tuberculosis surgery.

Table 1. General Information of Patients in the Surgical Site and Non-Surgical Site Infection Groups

	Non-surgical site infection (n = *318*)	*Surgical site infection* (n = *76*)	*Overall* (n = *394*)
Gender			
Female	131 (41%)	21 (28%)	152 (39%)
Male	187 (59%)	55 (72%)	242 (61%)
BMI	20.0 ± 2.55	20.1 ± 3.18	20.06 ± 2.68
Weight loss (kg)	2.33 ± 3.28	1.91 ± 3.09	2.25 ± 3.24
ODI	18.1 ± 8.70	16.1 ± 5.89	17.69 ± 8.26
VAS	7.37 ± 1.53	7.17 ± 1.27	7.33 ± 1.48
Age	49.7 ± 18.0	47.1 ± 15.7	49.22 ± 17.63
Occupation			
Non-farmer	121 (38%)	31 (41%)	152 (39%)
Farmer	197 (62%)	45 (59%)	242 (61%)
Race			
Non-Han	156 (49%)	38 (50%)	194 (49%)
Han	162 (51%)	38 (50%)	200 (51%)
Days before surgery (d)	5.23 ± 5.65	4.54 ± 3.23	5.09 ± 5.27
Systolic blood pressure (mm Hg)	127 ± 19.9	126 ± 18.1	126.47 ± 19.54
Diastolic blood pressure (mm Hg)	78.9 ± 11.4	77.1 ± 12.1	78.56 ± 11.57
Pain			
No	22 (7%)	1 (1%)	23 (6%)
Yes	296 (93%)	75 (99%)	371 (94%)
Lower limb pain			
No	149 (47%)	37 (49%)	186 (47%)
Yes	169 (53%)	39 (51%)	208 (53%)
Number of lower limbs with pain	0.925 ± 0.923	0.842 ± 0.895	0.91 ± 0.92
Fatigue			
No	221 (69%)	57 (75%)	278 (71%)
Yes	97 (31%)	19 (25%)	116 (29%)
Fever			
No	225 (71%)	58 (76%)	283 (72%)
Yes	93 (29%)	18 (24%)	111 (28%)
Night sweats			
No	243 (76%)	60 (79%)	303 (77%)
Yes	75 (24%)	16 (21%)	91 (23%)
Appetite			
No	132 (42%)	25 (33%)	157 (40%)
Yes	186 (58%)	51 (67%)	237 (60%)
Medical history (mo)	9.21 ± 17.3	6.12 ± 7.27	8.61 ± 15.89
ASIA			
A	3 (1%)	0 (0%)	3 (1%)
B	6 (2%)	0 (0%)	6 (2%)
C	25 (8%)	2 (3%)	27 (7%)
D	76 (24%)	16 (21%)	92 (23%)
E	208 (65%)	58 (76%)	266 (68%)
JOA	18.1 ± 6.21	18.9 ± 4.36	18.24 ± 5.90

BMI = body mass index; ODI = Oswestry Disability Index; VAS = visual analogue scale; ASIA = American Spinal Injury Association; JOA = Japanese Orthopedic Association.

A nomogram is often used to construct clinical prediction models to study the risk factors of events [13,14]. Hence, we used a nomogram for the first time to predict the risk of surgical site infection after spinal tuberculosis surgery. Also, it is clinically significant for surgeons in fully understanding the patient's parameters and assessing the risk of postoperative surgical site infections.

Patients and and Methods

This study was approved by the hospital ethics committee. Between June 2012 and June 2021, we used the electronic case database to collect the clinical data of patients with spinal tuberculosis who underwent surgery in our hospital. The inclusion criteria were: diagnosis of spinal tuberculosis by pathologic examination; no other infectious lesions before surgery; no history of spinal surgery, and complete clinical data. The exclusion criteria were: no spinal tuberculosis found by pathologic examination; other infectious lesions before surgery; history of spinal surgery, and incomplete clinical data. Surgical site infection was defined as red and swollen appearance with continuous discharge of pus after surgery and secretions being positive for tuberculosis acid-fast bacilli. All data were collected anonymously.

The patients were admitted to the anesthesia induction room one hour before surgery for anesthesia preparation and injected with cefuroxime 30 minutes before surgery to prevent infection. The operating door remained closed until the end of the operation.

Data collection

The clinical data of 394 patients with spinal tuberculosis who underwent surgery in our hospital were collected. Two hundred forty-two were males and 152 were females. The general information of such patients is listed in Table 1, including the Japanese Orthopedic Association scores (JOA), visual analogue scale (VAS), American Spinal Injury Association (ASIA), Oswestry Disability Index (ODI), days before surgery, gender, medical history, systolic blood pressure, diastolic blood pressure, body mass index (BMI), pain, lower limb pain, the number of lower limbs with pain, fatigue, fever, night sweats, weight loss, drinker, smoker, surgical approach, titanium cage, internal fixation, age, occupation, race, hypertension, diabetes, abscess, kyphosis, and lesion segment.

The laboratory test results recorded in this study (Table 2) were as follows: total protein, albumin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), AST/ALT,

Table 2. Laboratory Test Results of the Patients in the Surgical Site Infection and Non-Surgical Site E Groups

	Non-surgical site infection (n = *318*)	*Surgical site infection* (n = *76*)	*Overall* (n = *394*)
Blood glucose (mmol/L)	5.32 ± 1.39	5.03 ± 1.11	5.27 ± 1.35
Blood type			
A	61 (19%)	14 (18%)	75 (19%)
B	80 (25%)	23 (30%)	103 (26%)
AB	18 (6%)	6 (8%)	24 (6%)
O	159 (50%)	33 (43%)	192 (49%)
C-reactive protein (mg/L)	26.8 ± 35.1	38.7 ± 51.3	29.07 ± 38.98
Hepatitis B surface antigen			
Negative	285 (90%)	68 (89%)	353 (90%)
Positive	33 (10%)	8 (11%)	41 (10%)
White blood cells (*10^9/L)	7.16 ± 2.56	7.66 ± 3.42	7.24 ± 2.73
Hemoglobin (g/L)	121 ± 16.0	118 ± 19.2	120.76 ± 16.72
Platelets (*10^9/L)	308 ± 100	311 ± 115	308.43 ± 103.25
Percentage of neutrophils (%)	0.625 ± 0.115	0.643 ± 0.150	0.63 ± 0.12
Percentage of lymphocytes (%)	0.242 ± 0.104	0.217 ± 0.110	0.24 ± 0.11
Absolute monocytes (*10^9/L)	0.651 ± 0.273	0.667 ± 0.260	0.65 ± 0.27
Percentage of monocytes (%)	0.0994 ± 0.0672	0.0933 ± 0.0312	0.098 ± 0.062
Total bilirubin (mcmol/L)	8.33 ± 7.57	8.37 ± 9.75	8.34 ± 8.02
Direct bilirubin (mcmol/L)	3.49 ± 3.87	3.97 ± 6.27	3.58 ± 4.43
Indirect bilirubin (mcmol/L)	4.86 ± 4.09	4.41 ± 3.75	4.77 ± 4.02
Total protein (g/L)	70.7 ± 7.81	69.7 ± 7.13	70.5 ± 7.69
Albumin (g/L)	38.7 ± 4.65	36.9 ± 4.61	38.33 ± 4.69
AST (U/L)	25.9 ± 19.0	25.5 ± 22.9	25.83 ± 19.75
ALT (U/L)	23.7 ± 22.3	23.9 ± 24.4	23.74 ± 22.66
AST/ALT	1.50 ± 2.13	1.32 ± 0.629	1.47 ± 1.93
Blood uric acid (mcmol/L)	399 ± 183	405 ± 151	399.95 ± 177.42
Erythrocyte sedimentation rate (mm/h)	40.3 ± 27.8	39.8 ± 24.4	40.22 ± 27.13
Blood creatinine (mcmol/L)	70.1 ± 47.7	64.3 ± 14.5	68.99 ± 43.40
Blood urea (mmol/L)	4.44 ± 2.00	4.84 ± 2.43	4.52 ± 2.09

AST = aspartate aminotransferase; ALT = alanine aminotransferase.

Table 3. Surgical Information of the Patients in the Surgical Site Infection and Non-Surgical Site Infection Groups

	Non-surgical site infection (n = *318*)	*Surgical site infection* (n = *76*)	*Overall* (n = *394*)
Albumin quantity (bottle)	0.843 ± 2.17	1.28 ± 2.63	0.93 ± 2.27
Surgical approach			
Anterior	199 (63%)	42 (55%)	241 (61%)
Posterior	114 (36%)	32 (42%)	146 (37%)
Combined anterior and posterior	5 (2%)	2 (3%)	7 (2%)
Titanium cage			
No	174 (55%)	43 (57%)	217 (55%)
Yes	144 (45%)	33 (43%)	177 (45%)
Internal fixation			
No	39 (12%)	12 (16%)	51 (13%)
Yes	279 (88%)	64 (84%)	343 (87%)
Blood transfusion			
No	221 (69%)	49 (64%)	270 (69%)
Yes	97 (31%)	27 (36%)	124 (31%)
Local streptomycin			
No	44 (14%)	7 (9%)	51 (13%)
Yes	274 (86%)	69 (91%)	343 (87%)
Operation time (min)	126 ± 41.9	166 ± 87.3	133.68 ± 55.81
Bleeding volume (mL)	374 ± 367	503 ± 499	398.81 ± 398.76
Red blood cell transfusion (U)	0.893 ± 2.08	6.38 ± 45.8	1.95 ± 20.21
Drainage (mL)	329 ± 274	396 ± 357	342.29 ± 292.50
Abscess			
No	85 (27%)	10 (13%)	95 (24%)
Yes	233 (73%)	66 (87%)	299 (76%)
Kyphosis			
No	170 (53%)	39 (51%)	209 (53%)
Yes	148 (47%)	37 (49%)	185 (47%)
Incision length (cm)	9.40 ± 3.20	11.0 ± 4.99	9.72 ± 3.66
Lesion segment	2.12 ± 0.702	2.47 ± 1.14	2.19 ± 0.82

blood type, C-reactive protein (CRP), hepatitis B surface antigen, erythrocyte sedimentation rate, white blood cells, hemoglobin, platelets, percentage of neutrophils, percentage of lymphocytes, absolute monocytes, percentage of monocytes, total bilirubin, direct bilirubin, indirect bilirubin, blood urea, and blood uric acid. The surgical information (Table 3), including operation time, bleeding volume, red blood cell transfusion, albumin quantity, and incision length were collected.

Statistical analysis

All data were included in the least absolute shrinkage and selection operator (LASSO) regression analysis, and the selected parameters were analyzed using logistic regression and receiver operating characteristic (ROC) curve analysis. Statistically different parameters were used to construct the nomogram. To evaluate the deviation between the ideal value

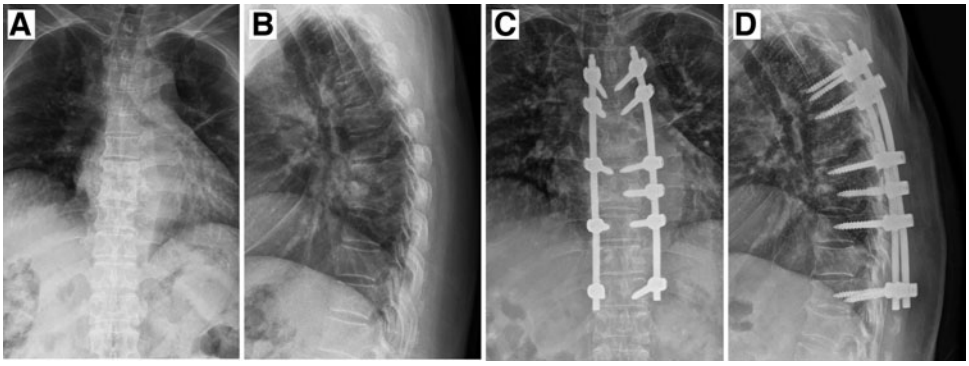

FIG. 1. Radiographic examination of the patient with surgical site infection. (**A**) Pre-operative radiograph in the posterior-anterior position. (**B**) Pre-operative radiograph in the lateral position. (**C**) Post-operative radiograph in the posterior-anterior position. (**D**) Post-operative radiograph in the lateral position.

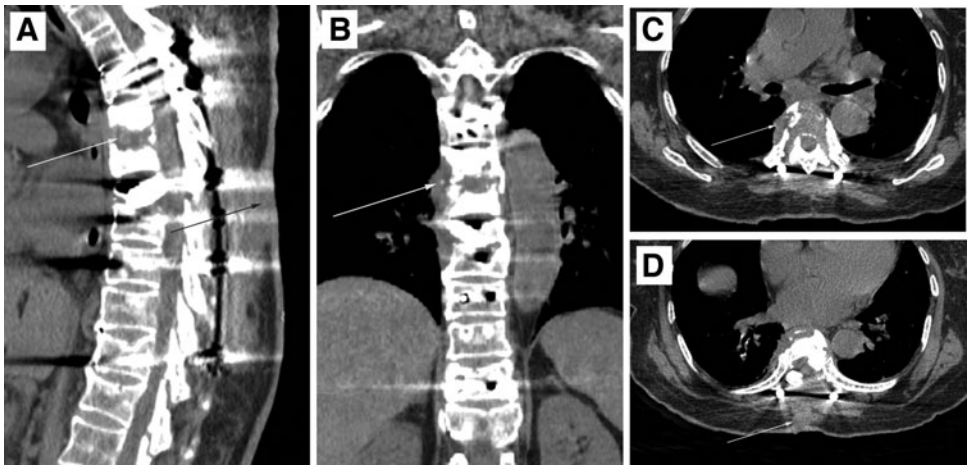

FIG. 2. Computed tomograpy (CT) examination of the patient with surgical site infection. (**A**) Post-operative CT image in the sagittal position. The top arrow points to the pus in the thoracic 5/6 intervertebral space and the lower arrow points to the pus under the skin. (**B**) Post-operative CT image in the coronal position. The arrow points to the paravertebral abscess. (**C**) Post-operative CT image in cross-section. The arrow points to the paravertebral abscess. (**D**) Post-operative CT image in cross-section. The arrow points to the pus under the skin.

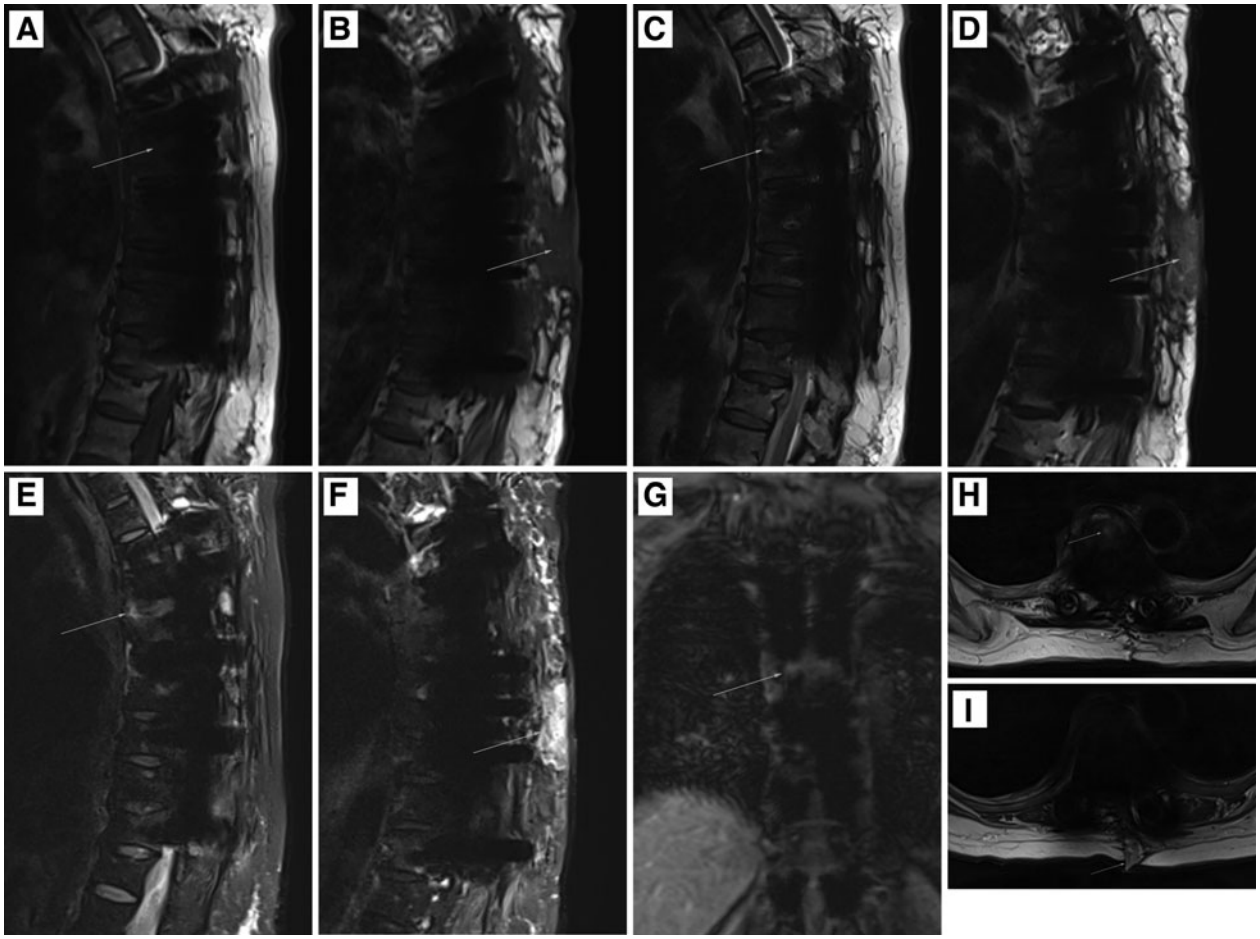

FIG. 3. Magnetic resonance imaging (MRI) examination of the patient with surgical site infection. (**A**) Post-operative MRI image in the sagittal T1 sequence. The arrow points to the pus in the thoracic 5/6 intervertebral space. (**B**) Post-operative MRI image in the sagittal T1 sequence. The arrow points to the pus under the skin. (**C**) Post-operative MRI image in the sagittal T2 sequence. The arrow points to the pus in the thoracic 5/6 intervertebral space. (**D**) Post-operative MRI image in the sagittal T2 sequence. The arrow points to the pus under the skin. (**E**) Post-operative MRI image of the T2 lipid compression sequence in sagittal position. The arrow points to the pus in the thoracic 5/6 intervertebral space. (**F**) Post-operative MRI image of the T2 lipid compression sequence in sagittal position. The arrow points to the pus under the skin. (**G**) Post-operative MRI image in the coronal position. The arrow points to the pus in the thoracic 5/6 intervertebral space. (**H**) Post-operative MRI image in cross-section. The arrow points to the pus in the thoracic 5/6 intervertebral space. (**I**) Post-operative MRI image in cross-section. The arrow points to the pus under the skin.

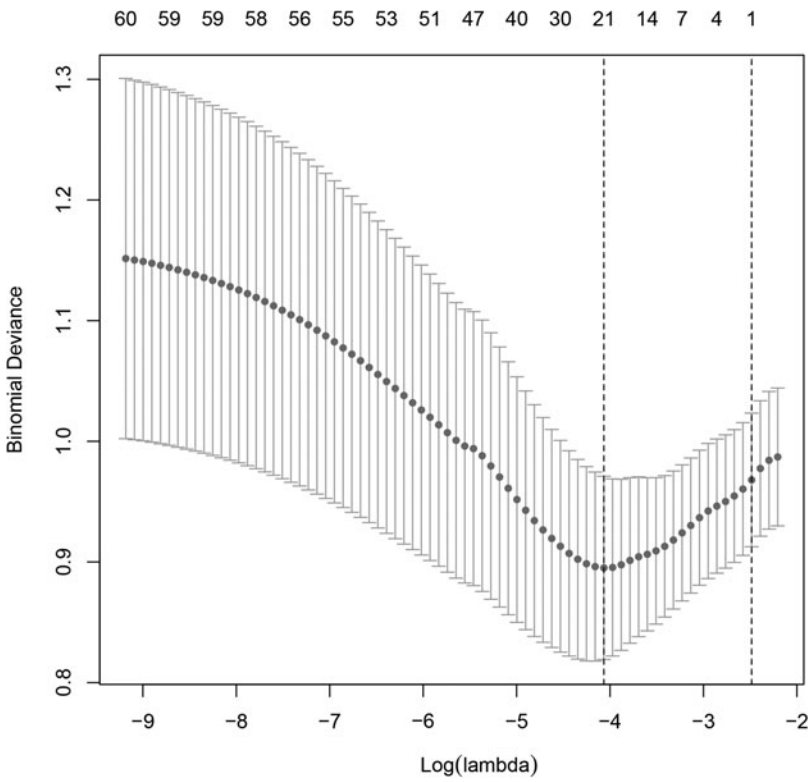

FIG. 4. The construction of the least absolute shrinkage and selection operator (LASSO) model for selecting the optimal parameters (λ) and drawing the relation graph between binomial deviance and log (λ).

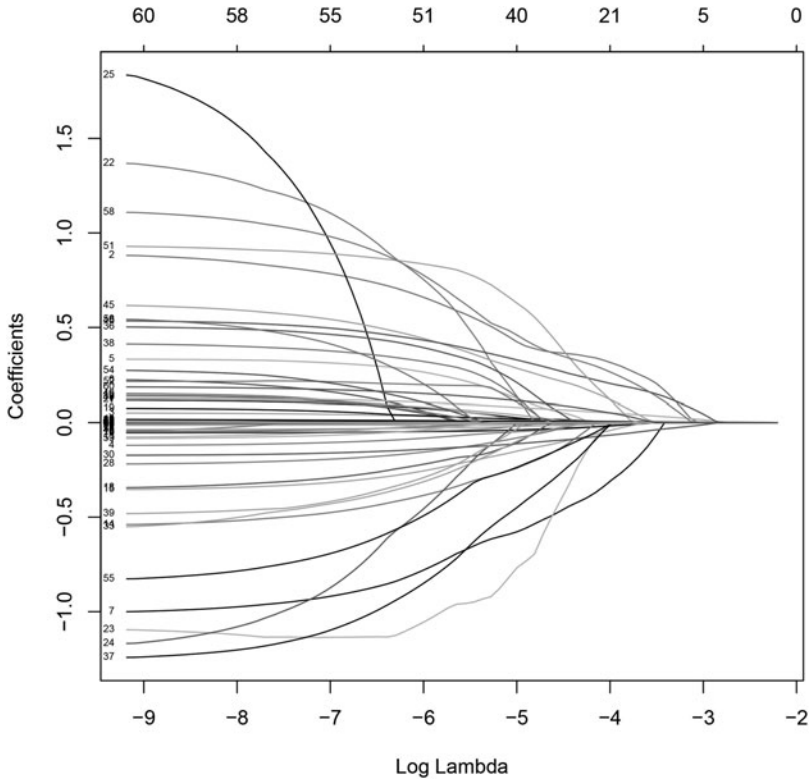

FIG. 5. The features with non-zero coefficients selected using optimal lambda.

Table 4. Multivariate Logistic Regression Analysis

	OR	*95%CI*	*P*
Albumin	0.872	0.804–0.942	0.001*
Operation time	1.013	1.007–1.019	< 0.001*
Incision length	1.104	1.014–1.208	0.025**
Lesion segment	1.477	1.019–2.166	0.042**
Medical history	0.960	0.917–0.994	0.047**
Blood urea	1.206	1.042–1.406	0.012**

OR = odds ratio; CI = confidence interval.
*p < 0.01; **p < 0.05.

and the actual value, a calibration curve was constructed, while to evaluate the discrimination of the nomogram, the area under the curve (AUC) and C-index were calculated. The net benefit was calculated using decision curve analysis (DCA). To evaluate the accuracy of the prediction model by bootstrapping with 1,000 resamples, we used the internal verification method to calculate the C-index. R, version 4.1 (R Foundation, Vienna, Austria) and RStudio, version 1.4 (RStudio, Boston, MA) software were used for statistical analysis. A p value <0.05 was considered statistically significant.

Results

Initially, we screened 732 patients with spinal tuberculosis. However, 237 and 101 patients were excluded because of incomplete data and poorly described surgical site information, respectively. A total of 394 patients with spinal tuberculosis surgery were included in the study, including 76 patients with surgical site infection and 318 patients without surgical site infection. The typical case of surgical site infection is shown in Figures 1 to 3. The patient's surgical sites were swollen and exuded pus after the surgery but healed well after a second debridement. The LASSO model was constructed to select the optimal parameters (λ) and draw the relation graph between binomial deviance and log (λ) (Fig. 4). The features with non-zero coefficients were selected using optimal λ (Fig. 5). The parameters selected by LASSO were included in the multivariable logistic regression analysis (Table 4) and also in the ROC curve analysis (Fig. 6 and Table 5). Albumin (p = 0.01), operation time (p = 0.001), incision length (p = 0.01), and lesion segment (p = 0.028) were found to have statistical differences. Additionally, albumin in patients with surgical site infection was lower than that in patients without surgical site infection (Fig. 7A). However, the operation time (Fig. 7B), lesion segment (Fig. 7C), and incision length (Fig 7D) were found to be higher in the surgical site infection group than in the non-surgical site infection group.

The nomogram in this study showed that the predicted risk of surgical site infection ranged between 0.01 and 0.98 (Fig. 8). The calibration curve showed rough consistency between the predicted value and the actual value (Fig. 9). The C-index of the nomogram (95% confidence interval [CI],

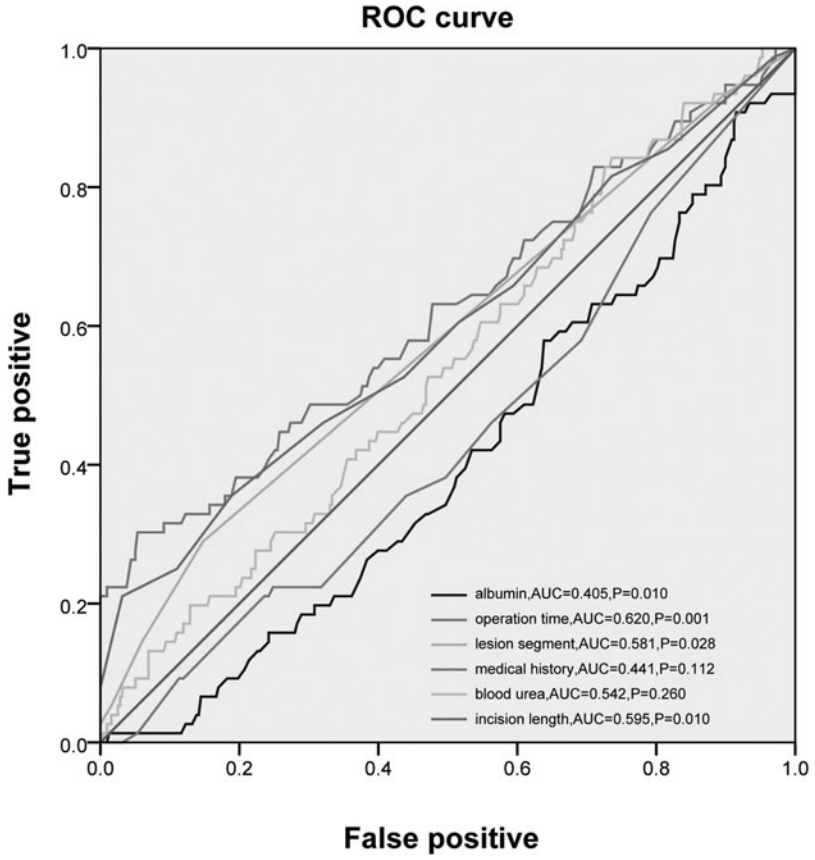

FIG. 6. The parameters, including albumin, blood urea, operation time, incision length, medical history, and lesion segment, analyzed by the receiver operating characteristic (ROC) curve.

Table 5. The AUC for the Parameters Was Calculated Using the ROC Curve

	AUC	95%CI	P
Albumin	0.405	0.336–0.473	0.010*
Operation time	0.620	0.544–0.697	0.001**
Incision length	0.595	0.518–0.571	0.010*
Lesion segment	0.581	0.507–0.656	0.028*
Medical history	0.441	0.370–0.512	0.112
Blood urea	0.542	0.471–0.613	0.260

AUC = area under the curve; ROC = receiver operating characteristic curve.
*$p < 0.05$; **$p < 0.01$.

0.62–0.76) and the AUC were found to be 0.69 (Fig. 10). The net benefit of the model determined by the DCA curve ranged between 0.01 and 0.99 (Fig. 11). The C-index calculated using the internal verification method of the nomogram was 0.68, which was almost identical to the C-index of the training set.

Before obtaining the results of drug susceptibility, we chose cefuroxime based on our experience to treat patients with surgical site infections. On obtaining the drug susceptibility results, we chose antibiotic agents sensitive to bacteria according to the results. The most common micro-organisms found in the bacterial culture of surgical site secretions were *Staphylococcus epidermidis*, *Staphylococcus aureus*, and *Clostridium perfringens*.

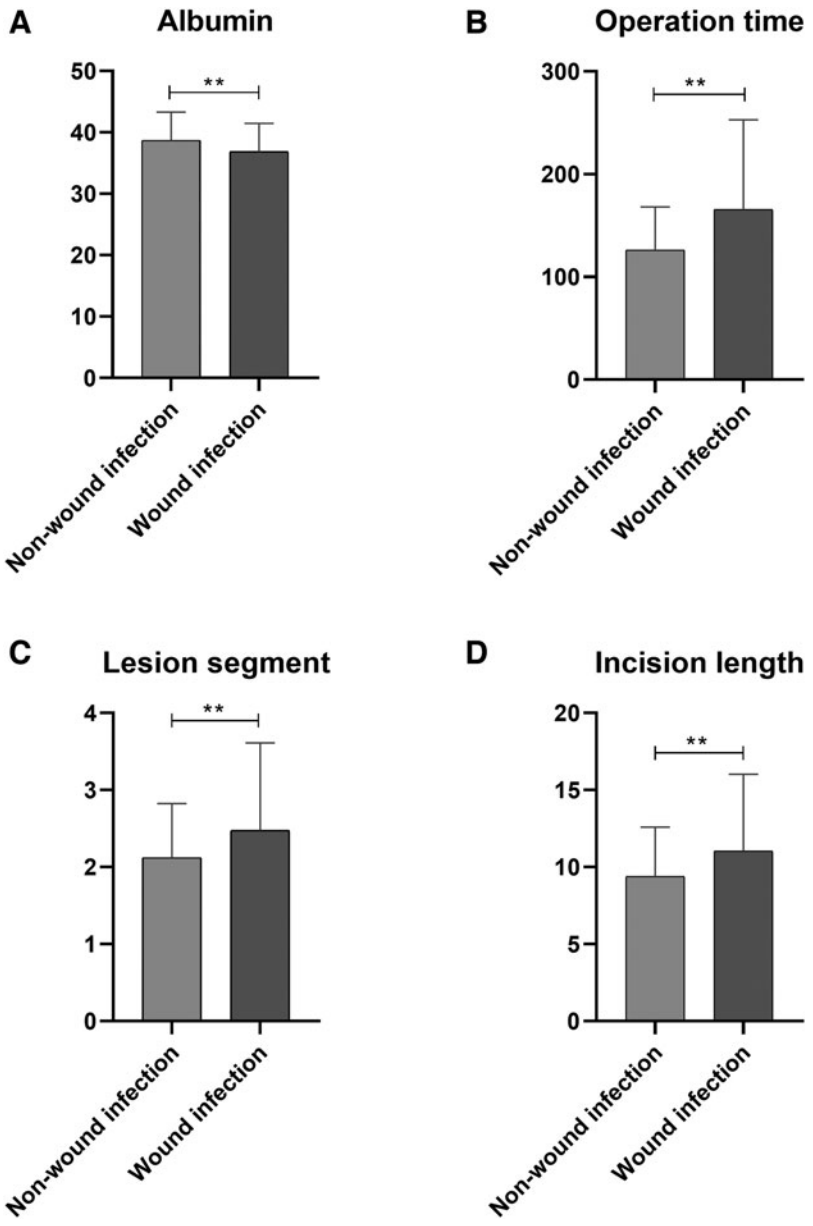

FIG. 7. Comparison of parameters between the surgical site and non-surgical site infection group. (**A**) Albumin. (**B**) Operation time. (**C**) Lesion segment. (**D**) Incision length. Note: *$p < 0.05$. **$p < 0.01$.

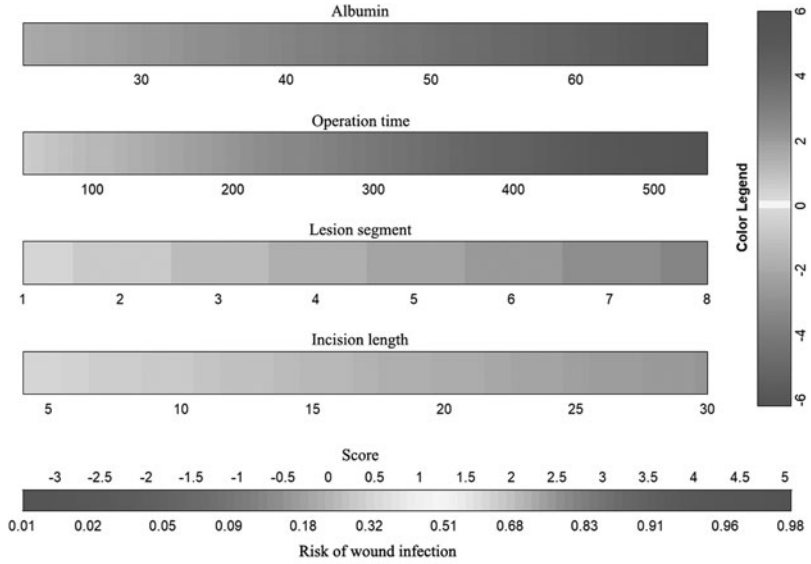

FIG. 8. The nomogram for predicting the risk of surgical site infection.

Discussion

The spine tuberculosis surgery methods usually include an anterolateral approach, a posterior approach, and a combined anterior and posterior approach [6,15]. The common postoperative surgical site complications include surgical site infection, delayed surgical site healing, and sinus tract [7–10,15]. Only a few reports are available in the literature on the risk factors of surgical site infection after spinal tuberculosis surgery. Hence, we constructed a nomogram to predict such risk factors.

The nomogram is widely used in clinical medical research to construct clinical prediction models [13,14], and the most significant predictive features are selected using the LASSO method [16,17]. Furthermore, the logistic regression analysis was used to fit the features with non-zero coefficients in the LASSO regression model [18]. We selected four parameters to construct the nomogram in this study. Based on the regression coefficient of the independent variables, the nomogram established the scoring standards [19]. The accuracy of the nomogram was evaluated using the C-index [20], which was calculated based on the probability estimate that the

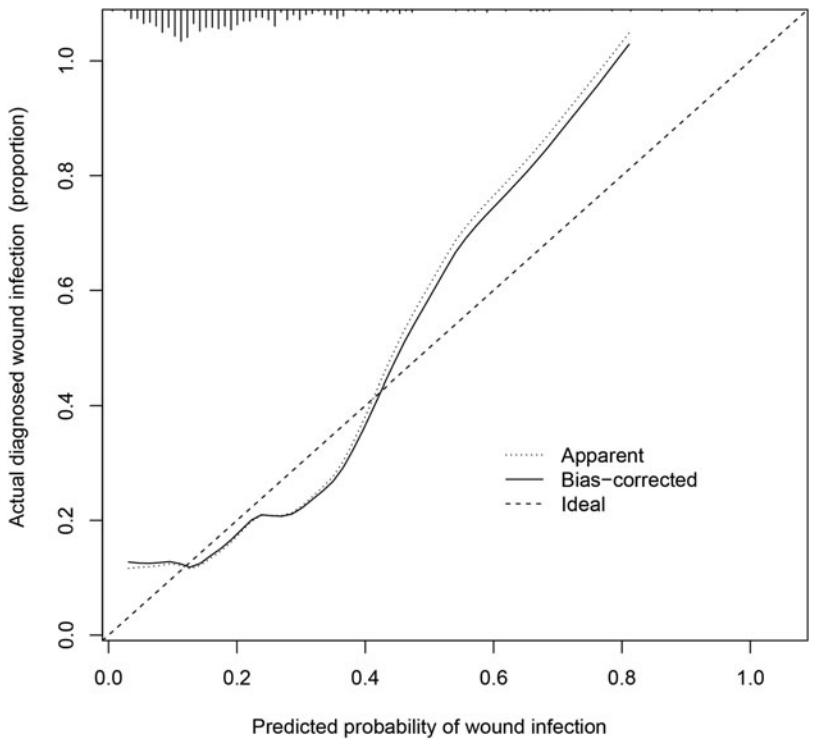

FIG. 9. Calibration curves for the nomogram of surgical site infection.

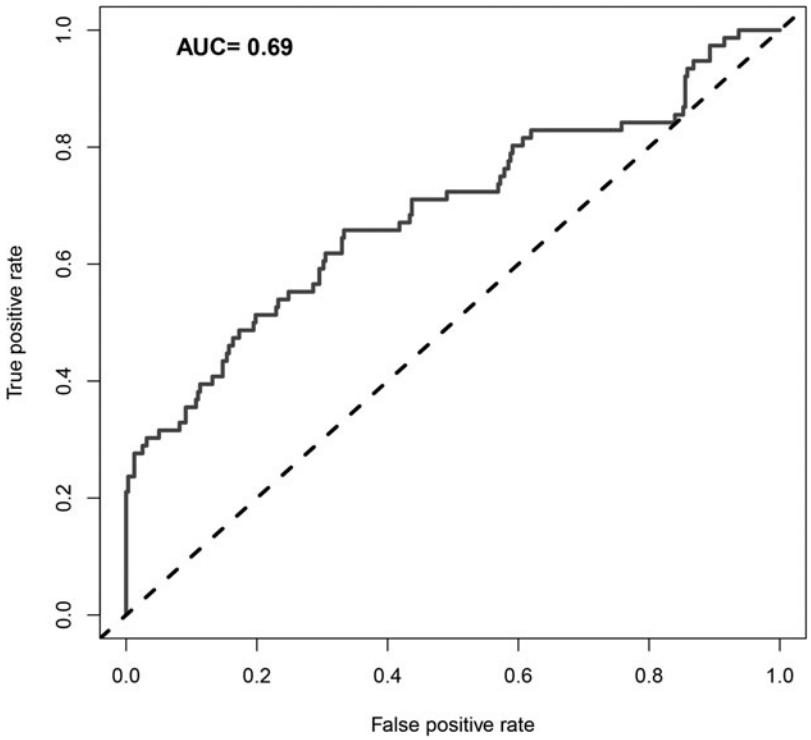

FIG. 10. Receiver operating characteristic (ROC) curve for the predictive nomogram. The area under the curve (AUC) value of the nomogram scoring system for predicting surgical site infection was 0.69.

predicted value was consistent with the actual value [21]. The C-index of the training set and the validation set in this study were 0.69 and 0.68, respectively. Generally, a C-index of 0.60 or higher is used to construct clinical prediction models [22]. To verify the accuracy of the nomogram, the AUC was calculated using the ROC curve [20]. Based on the potential clinical impact of biomarkers or models, DCA was recommended for the treatment or intervention [23]. The net benefit was calculated using the proportion of true positives minus the proportion of false positives weighted by the

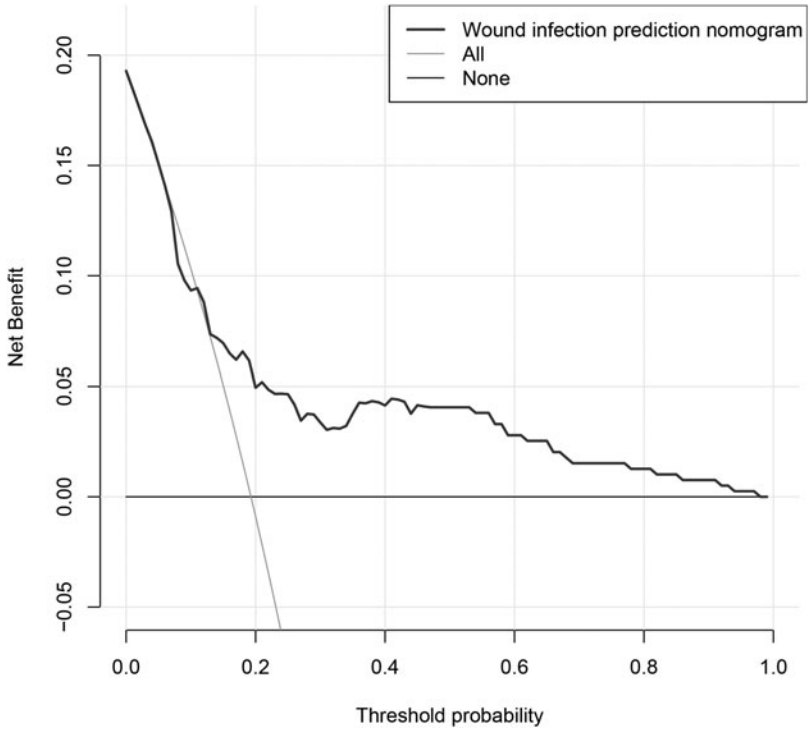

FIG. 11. The nomogram of the decision curve analysis (DCA) and the net benefit of the model ranging between 0.01 and 0.99.

relative harm of false-positive and false-negative results [20,24]. The net benefit of the model in our study ranged between 0.01 and 0.99.

Our results suggest that the operation time, incision length, and lesion segment could be used as predictors of surgical site infection after spinal tuberculosis surgery. Research by Yang et al. [8] showed that the operation time and incision length of the traditional group were higher than those of the minimally invasive group, with four cases of surgical site infection occurring in the former group but none in the latter. Consistent with our results, the study of Qian et al. [25] also showed that the incidence of surgical site infection was higher in the group with longer operation time. Similarly, Hersh et al. [26] showed that an increased incision length was accompanied by an increased risk of surgical site infection. Multi-lesion segments usually require a longer surgical incision to expose the operating field for adequately removing the lesions and implanting internal fixation devices. Moreover, the healing speed of long-segment surgical incisions was usually slower than that of the short-segment surgical incisions, with the infection rate of the former being higher than that of the latter [8]. Therefore, the multifocal segment may also be a risk factor for surgical site infection after spinal tuberculosis surgery.

Albumin is an important nutrient in the human body, which is important to maintain vascular osmotic pressure. In our study, albumin was found to be a predictor of surgical site infection. The lower the albumin, the higher the risk of surgical site infection is. The results of He et al. [27] supported our opinion, with the multivariable logistic regression analysis showing an albumin level of <35 g/L being a risk factor for post-operative surgical site infection [27]. A study on risk factors for surgical infection in 824 patients showed that albumin value <32 g/L could predict the incidence of infection after spinal surgery [28]. Tuberculosis causes poor appetite and insufficient nutritional intake in patients, resulting in low albumin. Therefore, such patients were prone to surgical site infection after surgery.

However, this study had some limitations. First, this research was a single-center study, and thus, multi-center data verification may be required. Second, the study only included the internal verification method. Hence, an external verification method may be needed in future studies.

Conclusions

The nomogram showed a good predictive ability. Albumin, lesion segment, operation time, and incision length were considered risk factors for predicting surgical site infection after spinal tuberculosis surgery.

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All procedures were performed in accordance with relevant guidelines. This article has been approved by the ethics committee of The First Affiliated Hospital of Guangxi Medical University. Written informed consent of patients has been obtained for this study.

Authors' Contributions

Liyi Chen wrote the article and prepared Figures 1 through 11 and Tables 1 through 5. All authors reviewed the article.

Data Availability

Data sharing is not applicable to this article because no datasets were generated or analyzed during the current study.

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Author Disclosure Statement

All authors declare no conflicts of interest.

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