

Predictive modeling for identifying infection risk following spinal surgery: Optimizing patient management

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Abstract. Infection is known to occur in a substantial proportion of patients following spinal surgery and predictive modeling may provide a useful means for identifying those at higher risk of complications and poor prognosis, which could help optimize pre- and postoperative management strategies. The outcome measure of the present study was to investigate the occurrence of all-cause infection during hospitalization following scoliosis surgery. To meet this aim, the present study retrospectively analyzed 370 patients who underwent surgery at the Second Affiliated Hospital, Zhejiang University School of Medicine (Hangzhou, China) between January 2016 and October 2022, and patients who either experienced or did not experience all-cause infection while in hospital were compared in terms of their clinicodemographic characteristics, surgical variables and laboratory test results. Logistic regression was subsequently applied to data from a subset of patients in order to build a model to predict infection, which was validated using another subset of patients. All-cause, in-hospital postoperative infections were found to have occurred in 66/370 patients (17.8%). The following variables were included in a predictive model: Sex, American Society of Anesthesiologists (ASA) classification, body mass index (BMI), diabetes mellitus, hypertension, preoperative

levels of white blood cells and preoperative C-reactive protein (CRP) and duration of surgery. The model exhibited an area under the curve of 0.776 against the internal validation set. In conclusion, dynamic nomograms based on sex, ASA classification, BMI, diabetes mellitus, hypertension, preoperative levels of white blood cells and CRP and duration of surgery may have the potential to be a clinically useful predictor of all-cause infection following scoliosis. The predictive model constructed in the present study may potentially facilitate the real-time visualization of risk factors associated with all-cause infection following surgical procedures.

Introduction

Adult spinal deformity, also termed scoliosis, affects 2-3% of the global population (1). It can be effectively treated in a large number of patients through surgery; however, the procedure is associated with a relatively high incidence of postoperative complications, such as infection, pain, impaired neurological function, muscle atrophy and the need for repeated surgery (2,3). It has been reported that up to 16% of patients may be diagnosed with an infection following surgery (4), which prolongs hospitalization, makes treatment more expensive and increases the risk for repeated surgery or even mortality (5,6). Several predictors of postoperative spinal infection have been identified, including male sex (7) and the American Society of Anesthesiologists (ASA) classification (8), in addition to obesity, hypertension and diabetes (9,10).

Numerous studies have been conducted to ascertain the risk factors associated with infection following scoliosis; however, these investigations have failed to effectively translate their findings into practical risk scales or predictive models (11-13). Moreover, the emphasis of prior scholarly articles has predominantly been focused on the association between patients' clinical characteristics and postoperative infection, with only limited attention given to the integration of patients' characteristics and laboratory tests in investigating the associated risk (14,15). Within the field of clinical practice, at present, the significance of these identified factors (such as smoking, obesity and operating times) appears to have been inadequately acknowledged by clinicians and anesthesiologists, as they are

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Abbreviations: ASA, American Society of Anesthesiologists; AUC, area under the curve

Key words: spinal surgery, prediction model, infection, scoliosis, dynamic nomogram

predominantly considered in isolation. Consequently, both the intuitive and practical utilization of these risk factors makes it challenging to ascertain the probability of a patient developing a postoperative infection.

Based on the aforementioned considerations, the aim of the present study was to examine the perioperative risk factors associated with postoperative infection in individuals undergoing scoliosis surgery. Subsequently, an intuitive nomogram model to forecast the likelihood of infection following scoliosis surgery was devised and validated.

Patients and methods

Patients. In the present study, a consecutive sample of adults with non-degenerative scoliosis, who underwent internal fixation and spinal fusion surgery via the conventional midline open posterior approach between January 2016 and October 2022 at the Department of Orthopedic Surgery of the Second Affiliated Hospital of Zhejiang University School of Medicine (Hangzhou, China), were retrospectively analyzed. The patient inclusion criteria for the present study were as follows: i) Age >45 years; and ii) a primary Cobb angle ≥ 20 . The patient exclusion criteria were defined as: i) A diagnosis of degenerative or new-onset scoliosis, usually defined as degenerative changes in the lumbar spine without pre-existing scoliosis; ii) other types of spinal deformities, including ankylosing spondylitis, spinal tumors, medically induced spondylolisthesis or post-traumatic spondylolisthesis; iii) a history of lumbar spine surgery, anterior internal fixation or non-fusion surgery; and iv) incomplete pre- or postoperative imaging data (Fig. S1). The present cohort had 70 males and 300 females with a mean age at surgery of 65.5 years (range, 45–84 years). Concerning the use of antibiotics during the perioperative period, antibiotics (cefepodoxime) were routinely administered to relevant patients prior to surgery. The antibiotics were administered intravenously before the operation and every 2 h during the operation. On the first day after surgery, second-generation cephalosporin (such as ceftriaxone) was routinely administered intravenously at a dose of 1.5 g twice a day for 48 h. If the patient was allergic, administer 1,200 mg clindamycin was administered intravenously twice a day for 48 h.

The present study was approved by the Ethics Committee of the Second Affiliated Hospital of Zhejiang University School of Medicine (approval no. 2022-0968; Hangzhou, China). The requirement for informed consent was waived, since all the patients at the time of surgery provided written consent for their anonymized medical data to be analyzed and published for research purposes.

Exploratory data analyses. When selecting variables, correlations between variables were assessed using the Pearson correlation coefficient, a heatmap (Fig. S2) was constructed and the association between variables was analyzed, revealing that no correlation existed among the included variables [sex, age, body mass index (BMI), smoking, alcohol consumption, ASA class, previous surgical history, hypertension, diabetes mellitus, hypoproteinemia, coronary heart disease (CHD), hypohepatia, renal insufficiency, preoperative hemoglobin (pre-HB), preoperative white blood cell count (pre-WBC), preoperative albumin (pre-ALB), preoperative creatinine

(pre-Cr), preoperative c-reactive protein (pre-CRP), preoperative glutamic-pyruvic transaminase, preoperative aspartate aminotransferase, Cobb angle, the number of fused segments during surgery, homologous blood transfusion, surgical duration and intraoperative blood loss).

In addition, monotonicity testing was performed on the continuous variables in the modeling and a restricted cubic spline was created (Figs. S3–6). These graphs demonstrate a linear relationship between the continuity variables used for modeling and postoperative infections.

Definition of the outcome. The outcome was defined as the occurrence of all-cause, in-hospital infection following surgery. Such infections were diagnosed based on the criteria for surgical site, urinary tract or respiratory tract infection published as European Perioperative Clinical Outcome definitions (16). Superficial incisional surgical site infection was defined by the following criteria (16): i) Infection occurring ≤ 30 days after surgery; ii) limited to the skin and subcutaneous tissue of the incision; and iii) presence of at least one of the following: (a) Purulent drainage from the superficial incision; (b) isolation of organisms from an aseptically obtained culture of fluid or tissue from the superficial incision; (c) presence of infection-related symptoms or signs, such as pain or tenderness, localized swelling, redness or heat, along with deliberate opening of the superficial incision by a surgeon resulting in a positive culture (a culture-negative finding does not meet this criterion); or (d) diagnosis of a superficial incisional surgical site infection by a surgeon or attending physician. Deep incisional surgical site infection was characterized by the following criteria: i) Infection occurring ≤ 30 days after surgery if no implant was left in place or ≤ 1 year if an implant was present; ii) involvement of deep soft tissues including fascial and muscle layers of the incision; and iii) presence of at least one of the following: (a) purulent drainage from the deep incision, but not from the organ/space component of the surgical site; (b) spontaneous or deliberate opening of the deep incision by a surgeon with positive culture results, in the presence of symptoms such as fever ($>38^\circ\text{C}$) or localized pain or tenderness (a culture-negative finding does not meet this criterion); (c) identification of an abscess or other evidence of infection within the deep incision during direct examination, surgery or through histopathological or radiological examination; or (d) diagnosis of a deep incisional surgical site infection by a surgeon or attending physician.

A urinary tract infection was defined by a positive urine culture that comprised 1×10^5 colony-forming units/ml, which involved ≤ 2 microbial species and featured at least one of the following symptoms or signs: i) Fever ($>38^\circ\text{C}$); ii) urinary urgency; iii) excessive urination frequency; iv) dysuria; v) suprapubic tenderness; or vi) pain or tenderness in the vertebrocostal angle in the absence of any other symptoms or signs.

A respiratory tract infection was diagnosed if the patient had been treated with antibiotics for a suspected respiratory tract infection and showed at least one of the following: i) New or altered sputum; ii) new or altered atelectasis; iii) fever; or iv) a WBC count $>12 \times 10^9$ cells/ml.

Finally, infections of unknown type were diagnosed if there was strong clinical suspicion of infection at more than one possible infection site and at least two of the following were

present: i) A core temperature $<36.8^{\circ}\text{C}$ or $>38.8^{\circ}\text{C}$; ii) a white blood cell count $>12 \times 10^9$ or $<4 \times 10^9$ cells/ml; iii) a respiratory rate >20 breaths/min or partial pressure of carbon dioxide <4.7 kPa (35 mmHg); or iv) a pulse reading of >90 beats/min.

Candidate predictors. A comprehensive set of non-modifiable and modifiable sociodemographic, clinical and surgical factors was selected *a priori* as candidate predictors, based on their recognized clinical importance and a previously published study (5). The candidate predictors comprised of 21 preoperative variables and four surgical variables. Variables were included in the analysis if data were available for $>90\%$ of the patients after random forest imputation. The following demographic and clinical data for the patients were obtained: Sex, age, BMI, smoking, alcohol consumption, ASA class, previous surgical history, hypertension, diabetes mellitus, hypoproteinemia, CHD, hypohepatia, renal insufficiency, pre-HB, pre-WBC, pre-ALB, pre-Cr, pre-CRP, preoperative glutamic-pyruvic transaminase, preoperative aspartate aminotransferase, Cobb angle, the number of fused segments during surgery, homologous blood transfusion, surgical duration, intraoperative blood loss. Additionally, for all patients undergoing scoliosis surgery, before suturing the wound, the surgeon routinely rinsed the wound with disinfectant and placed a drainage tube. Postoperative drainage volume and catheter placement time were also noted, but since preoperative and intraoperative variables were used to predict postoperative infection, postoperative variables were not included in the analysis. In addition, data on postoperative infections were collected. All complications were recorded using the hospital's electronic records system.

Development and interval validation of the predictive model. All statistical analyses were performed using various packages in R (version 4.2.2; Posit), including rms (version 1.6.0), pROC, MASS, survival and dcurves. The sample size used in the present study complied with the events per variable principle (17). $P < 0.05$ was considered to indicate a statistically significant difference. Normally distributed continuous data are reported as the mean and standard deviation, whereas skewed continuous data are presented as median values [interquartile range, n (%)].

Enrolled patients were randomly divided into a training dataset and a validation dataset in a 3:1 ratio. Based on the training dataset, univariate associations were assessed for significance using either the Chi-square or Fisher's exact test in the case of categorical variables or using Welch's two-sample t-test or Wilcoxon's rank-sum test in the case of continuous variables. Covariance between variables was assessed using the variance inflation factor in the rms package and VIF values of ≥ 5 were defined to indicate multicollinearity. An events per variable ratio of 10 was applied to avoid overfitting. Multivariate analyses were performed using the least absolute shrinkage and selection operator (LASSO) regression analysis and the final predictive nomogram was built according to the minimum Akaike information criterion.

The risk of in-hospital, all-cause postoperative infection was expressed in terms of adjusted odds ratio and its corresponding 95% CI. Nomogram performance was assessed against the training and validation datasets in terms of the area

under the curve (AUC) and calibration curves. Finally, decision curve analysis was performed to determine the predicted net benefit threshold.

To facilitate incorporation of the nomogram into clinical practice, the nomogram was integrated into an interactive web-based application using Shiny (version 1.7.4; <https://nomoixtcljn.shinyapps.io/dynomapp/>).

Results

Demographics. Of the 370 patients used in the final analysis, 278 were included in the training dataset, whereas 92 were included in the validation dataset. The two datasets showed similar sex distribution, a median age of 66 years and a mean BMI of ~ 23 (Table I). The two datasets were not found to differ significantly in terms of any of the clinicodemographic characteristics that were examined.

Univariate analysis of all-cause, in-hospital infection. Univariate analysis of the training dataset was employed to identify the following significant associations between clinicodemographic characteristics and all-cause, in-hospital infection following surgery: ASA score, hypertension, diabetes mellitus, preoperative white blood cell count and preoperative level of CRP (Table II).

LASSO regression of the training dataset involving numerous variables identified eight that were significantly associated with infection and that did not significantly co-vary with one another, namely, sex, ASA score, BMI, hypertension, diabetes mellitus, preoperative white blood cell count, preoperative level of CRP and duration of surgery (Fig. 1). The final model showed a cross-validation error within one standard error of the minimum. The model was converted into a nomogram (Fig. 2), which was subsequently integrated into an online application to facilitate dissemination and external validation.

The AUC for the final model varied from 0.5 (no discriminant) to 1.0 (complete discriminant) across different subgroups within the training dataset and from 0.5 (no discriminant) to 1.0 (complete discriminant) within the validation dataset (Fig. 3). The calibration plots of the nomograms showed a good level of agreement in the comparison between observed and predicted rates of infections in the two datasets (Fig. 4).

To assess the clinical usefulness of the predictive model more rigorously, decision curve analysis with the final nomogram was performed. The regression coefficient β for each variable was obtained from multivariate logistic regression analysis and was converted into scores that were scaled from 0-100. The scores for each variable were summed to obtain a total score, indicating the probability of all-cause, in-hospital infection following surgery. The curves obtained showed relatively large differences between the rates of true positives and false negatives in both the training and validation datasets (Fig. 5), which suggested a high net benefit (18).

Discussion

In the present study, to the best of our knowledge for the first time, a dynamic nomogram was developed and internally validated for predicting all-cause infection in patients aged >45 years following scoliosis surgery. The dynamic nomogram

Table I. Patient demographics and baseline characteristics of the training and internal validation cohorts.

Patient characteristic	Training cohort (n=278)	Internal validation cohort (n=92)	P-value
Sex, n (%)			0.296
Male	56 (20)	14 (15)	
Female	222 (80)	78 (85)	
Median age, years (interquartile range)	66 (61-70)	66 (62-69)	0.643
Mean BMI, kg/m ² (standard deviation)	23.4 (3.4)	22.6 (3.4)	0.050
Smoking, n (%)			0.392
No	259 (93)	88 (96)	
Yes	19 (6.8)	4 (4.3)	
Alcohol consumption, n (%)			0.840
No	255 (92)	85 (92)	
Yes	23 (8.3)	7 (7.6)	
American Society of Anesthesiologists class, n (%)			0.658
I	3 (1.1)	2 (2.2)	
II	245 (88.0)	79 (86.0)	
III	30 (11.0)	11 (12.0)	
Previous surgical history, n (%)			0.173
No	214 (77.0)	77 (84.0)	
Yes	64 (23)	15 (16)	
Hypertension, n (%)			0.226
No	174 (63)	64 (70)	
Yes	104 (37)	28 (30)	
Diabetes mellitus, n (%)			0.058
No	257 (92)	79 (86)	
Yes	21.0 (7.6)	13.0 (14.0)	
Hypoproteinemia, n (%)			0.455
No	260 (94)	88 (96)	
Yes	18.0 (6.5)	4.0 (4.3)	
Hyperlipemia, n (%)			0.758
No	248 (89)	81 (88)	
Yes	30 (11)	11 (12)	
Hypohepatia, n (%)			>0.999
No	274 (99)	91 (99)	
Yes	4.0 (1.4)	1.0 (1.1)	
Renal insufficiency, n (%)			0.201
No	212 (76)	64 (70)	
Yes	66 (24)	28 (30)	

Data were analyzed using Pearson's Chi-square test, Wilcoxon rank-sum test, Welch's two-sample t-test or Fisher's exact test.

was based on patient sex, ASA score, BMI, diabetes mellitus, hypertension, preoperative levels of white blood cells and CRP and the duration of surgery. The model produced in the present study may contribute to the future establishment of a framework for the creation of a web-based, point-of-care tool for calculating in real time the risk of developing short-term infection following surgery. Such a tool may facilitate communication with patients to lessen the risk of postoperative infection.

Patients who undergo scoliosis surgery, frequently encounter an elevated susceptibility to postoperative

infection (2). The surgical procedure has the potential to compromise the body's innate immune system, as incisions and tissue manipulation establish routes through which pathogens may infect the patient (19). It is worth noting that due to the complexity of the surgery, scoliosis surgery may last for a long time, thereby prolonging the exposure of the wound to external factors and applying long-term tension to the tissue. This situation may result in localized hemorrhage and necrosis, while also increasing the patient's vulnerability to infection due to prolonged exposure to pathogens in a hospital environment (20). Furthermore, the ASA classification system

Table II. Single-factor analysis for predicting infection after scoliosis surgery in a training and an internal validation cohort of patients.

Patient characteristic	Training cohort			Internal validation cohort		
	0 (n=227)	1 (n=51)	P-value	0 (n=77)	1 (n=15)	P-value
Sex, n (%)			0.068			>0.999
Male	41 (18)	15 (29)		12 (16)	2 (13)	
Female	186 (82)	36 (71)		65 (84)	13 (87)	
Median age, years (IQR)	66.0 (61.0-70.0)	67.0 (62.0-72.0)	0.281	66.0 (62.0-69.0)	66.0 (64.0-69.5)	0.611
Mean BMI, kg/m ² (standard deviation)	23.3 (3.4)	24.1 (3.5)	0.168	22.6 (3.4)	22.6 (3.8)	0.954
Smoking, n (%)			0.359			>0.999
No	213 (94)	46 (90)		73 (95)	15 (100)	
Yes	14 (6.2)	5 (9.8)		4 (5.2)	0 (0)	
Alcohol consumption, n (%)			0.396			>0.999
No	210 (93)	45 (88)		71 (92)	14 (93)	
Yes	17 (7.5)	6 (12)		6 (7.8)	1 (6.7)	
American Society of Anesthesiologists class, n (%)			0.004			0.778
I	2 (0.9)	1 (2.0)		2 (2.6)	0 (0)	
II	207 (91)	38 (75)		65 (84)	14 (93)	
III	18.0 (7.9)	12.0 (24.0)		10.0 (13.0)	1.0 (6.7)	
Previous surgical history, n (%)			0.522			0.258
No	173 (76)	41 (80)		66 (86)	11 (73)	
Yes	54 (24)	10 (20)		11 (14)	4 (27)	
Hypertension, n (%)			0.011			0.376
No	150 (66)	24 (47)		55 (71)	9 (60)	
Yes	77 (34)	27 (53)		22 (29)	6 (40)	
Diabetes mellitus, n (%)			0.006			0.439
No	215 (95)	42 (82)		67 (87)	12 (80)	
Yes	12 (5.3)	9 (18)		10 (13)	3 (20)	
Hypoproteinemia, n (%)			0.112			0.516
No	215 (95)	45 (88)		74 (96)	14 (93)	
Yes	12.0 (5.3)	6.0 (12.0)		3.0 (3.9)	1.0 (6.7)	
Coronary heart disease, n (%)			0.430			>0.999
No	219 (96)	48 (94)		75 (97)	15 (100)	
Yes	8.0 (3.5)	3.0 (5.9)		2.0 (2.6)	0.0 (0)	
Hypohepatia, n (%)			0.558			>0.999
No	224 (99)	50 (98)		76 (99)	15 (100)	
Yes	3.0 (1.3)	1.0 (2.0)		1.0 (1.3)	0.0 (0)	
Renal insufficiency, n (%)			0.156			0.540
No	177 (78)	35 (69)		52 (68)	12 (80)	
Yes	50 (22)	16 (31)		25 (32)	3 (20)	
Median preoperative hemoglobin, g/l (IQR)	123 (111-134)	126 (109-134)	0.756	125 (111-134)	131 (117-134)	0.256
Median preoperative white blood cell count, x10 ⁹ /l (IQR)	5.40 (4.30-6.80)	6.70 (5.80-8.15)	<0.001	6.20 (4.80-7.50)	4.90 (4.40-6.20)	0.054
Median preoperative albumin, U/l (IQR)	39.3 (36.6-41.6)	39.4 (36.5-41.4)	0.810	38.8 (37.0-41.6)	40.1 (38.0-41.5)	0.489
Median preoperative aspartate aminotransferase, U/l (IQR)	22.0 (19.0-27.0)	23.0 (20.0-27)	0.949	22.0 (20.0-26.0)	20.0 (18.0-24.5)	0.244

Table II. Continued.

Patient characteristic	Training cohort			Internal validation cohort		
	0 (n=227)	1 (n=51)	P-value	0 (n=77)	1 (n=15)	P-value
Median preoperative creatinine, mmol/l (IQR)	57 (50-64)	61 (52-71)	0.157	56 (51-66)	58 (51-60)	0.874
Median preoperative C-reactive protein, mg/l (IQR)	3 (1-6)	4 (2-22)	0.014	4 (2-16)	2 (1-4)	0.098
Median preoperative glutamic-pyruvic transaminase, mmol/l (IQR)	4.85 (4.49-5.44)	5.04 (4.69-5.76)	0.061	4.99 (4.49-5.58)	5.04 (4.65-5.77)	0.604
Median Cobb angle, ° (IQR)	34 (27-41)	34 (30-40)	0.786	36 (29-44)	41 (32-47)	0.403
Median number of fused segments, n (IQR)	4.00 (2.95-6.00)	5.00 (3.00-6.00)	0.510	5.00 (3.00-6.00)	4.00 (4.00-6.00)	0.889
Homologous blood transfusion, n (%)			0.487			0.349
No	141 (62)	29 (57)		46 (60)	7 (47)	
Yes	86 (38)	22 (43)		31 (40)	8 (53)	
Median surgical duration, min (IQR)	200 (145-285)	215 (163-293)	0.280	185 (135-270)	215 (145-263)	0.783
Median intraoperative blood loss, ml (IQR)	300 (200-625)	400 (200-800)	0.429	300 (125-600)	300 (150-800)	0.782

Data were analyzed using Pearson's χ^2 test, Wilcoxon rank-sum test, Welch's two-sample t-test or Fisher's exact test. IQR, interquartile range.

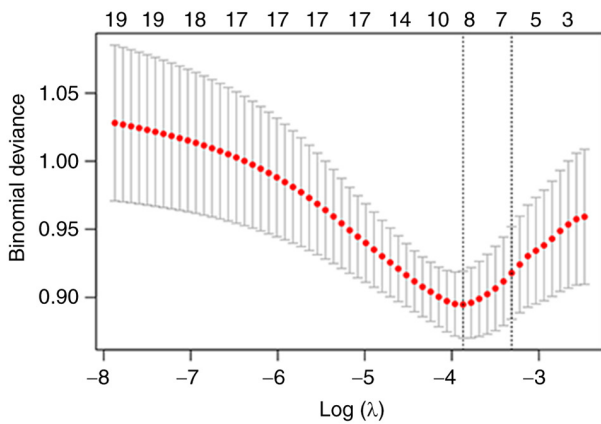


Figure 1. Least absolute shrinkage and selection operator regression cross-validation diagram indicating that the number of screened variables was eight.

is used to evaluate patients' preoperative health condition, with particular emphasis placed on the existence of comorbidities, such as diabetes and hypertension. Higher ASA scores are indicative of a diminished health status, which also correlates with an elevated likelihood of postoperative complications, including infections (21). Of particular significance is the fact that preoperative CRP is frequently employed for the identification of inflammatory processes, especially infections. Higher preoperative leukocyte and CRP levels have been shown to be correlated with an increased likelihood of postoperative infection in orthopedic surgery (22). The integration of preoperative CRP and leukocyte levels alongside

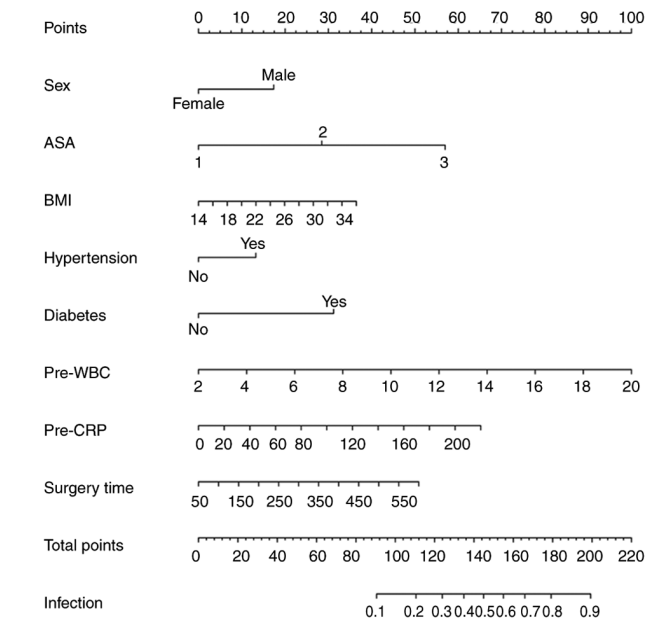


Figure 2. Intuitive nomogram of the variables selected by least absolute shrinkage and selection operator regression. ASA, American Society of Anesthesiologists; WBC, white blood cell count; CRP, C-reactive protein; pre, preoperative.

additional clinical parameters, such as the type of surgery and the patient's history, within a postoperative infection prediction model has the potential to enhance the precision in forecasting the probability of postoperative infection (23). When integrated into predictive models, these biomarkers

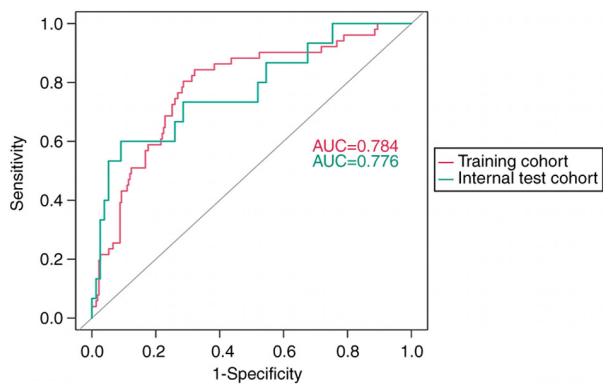


Figure 3. Area of the receiver operating characteristic curve of the prediction model with a training set of 0.784 and an internal validation set of 0.776. AUC, area under the curve.

provide some assistance for healthcare providers in terms of evaluating risk and implementing preventative measures to mitigate the occurrence of postoperative infections (24). For example, the administration of prophylactic antibiotics to mitigate preoperative inflammation levels can be employed to manage postoperative infections.

Ultimately, investigations into the association between the sex of the patient and postoperative infections subsequent to spine surgery have yet to yield conclusive findings. It has been shown that there may be a marginal increase in the susceptibility of male patients to postoperative infection (25). This phenomenon could potentially be attributed to variances in the levels of sex hormones, especially androgens, which have an impact on the immune response, or the fact that different surgery types are more likely to be performed on a particular sex (26). Subsequent investigations could explore the notion that stratifying the data according to the patient's sex may potentially offer a more comprehensive understanding of this phenomenon.

It is noteworthy that the final prediction model constructed in the present study did not incorporate variables that were previously shown to have strong associations with factors influencing postoperative complications, such as the number of surgical segments and intraoperative blood loss (27). The selection of variables in the present study was carried out with meticulous and deliberate consideration, placing emphasis on their statistical significance, predictive validity and the potential to enhance the overall accuracy of the model. Despite initially considering variables that were associated with the number of operated segments and intraoperative bleeding, these were ultimately excluded from the final prognostic model for postoperative complications. It was considered that the duration of surgery variable effectively encompassed both the influence and intricacy of the quantity of segments undergoing surgical intervention. Consequently, the incorporation of the 'number of segments operated' variable in the predictive model was deemed superfluous. Moreover, the integration of an inclusive intraoperative hemoprotection strategy assumed a pivotal role in the decision-making procedure. Methods such as autologous transfusion and isovolumic hemodilution were used to reduce blood loss during surgery (27). These measures have the potential to mitigate the impact of the 'intraoperative

bleeding' variable as an important prognostic indicator of postoperative complications. The exclusionary methodology adopted in the present study involved a comprehensive assessment of the individual prognostic value of these variables, their interrelationships and the efficacy of the surgical interventions employed. It was considered that these deliberations may potentially have significantly contributed to the development of the predictive model.

In order to mitigate these risks, the present study's hospital has implemented stringent infection control protocols, which include the administration of antibiotics during the perioperative period, the utilization of aseptic techniques during surgery and postoperative surveillance for any indications of infection (28). Furthermore, ongoing advancements in surgical methodologies and materials are being pursued with the objective of diminishing the probability of postoperative infections (29). However, the emergence of novel pathogens continues to present a formidable obstacle; consequently, healthcare facilities must modify their protocols and strategies to effectively confront these evolving threats. Additionally, an excessive or improper utilization of antibiotics can give rise to the proliferation of antibiotic-resistant bacteria, thereby exacerbating the complexities associated with the treatment of infection (30). This issue presents a substantial challenge for healthcare organizations, and therefore, the implementation of a predictive model incorporating both preoperative and intraoperative variables to anticipate postoperative infections in spinal surgery holds promise in terms of introducing transformative modifications to existing protocols. Concurrently, the provision of a more precise risk assessment could potentially assist healthcare providers in terms of enhancing their alertness for potential occurrences of postoperative infections.

Hospitals can improve their resource allocation efficiency by identifying patients who have a heightened susceptibility to infection, thereby enabling high-risk patients to receive higher levels of attention, monitoring and preventative measures, which could optimize resource utilization (31). Moreover, given the accumulating data in this area, the model constructed in the present study could undergo refinement and enhancement in the future to incorporate novel insights and factors that contribute to infection risk. This iterative process may facilitate a continuous improvement in the model's accuracy and reliability.

In recent years, nomograms have been widely used in clinical practice, and dynamic nomograms have increasing potential in terms of their effectiveness in being applied in the clinic (32). The dynamic nomogram that has been described in the present study was built from clinically readily available variables, thereby providing clinicians with continuously updated risk assessments for patients based on their changing clinical parameters. Through an understanding of these factors, clinicians will be more able to stratify patients according to their risk of developing infections, with the subsequent implementation of appropriate preventative measures. Moreover, the present model could potentially provide a quantitative tool for clinicians to predict postoperative infection more accurately, aiding in improved risk stratification. Additionally, a website was created for the present model (<https://nomoixtcljn.shinyapps.io/dynnomapp/>), with the aim to facilitate its application for surgeons

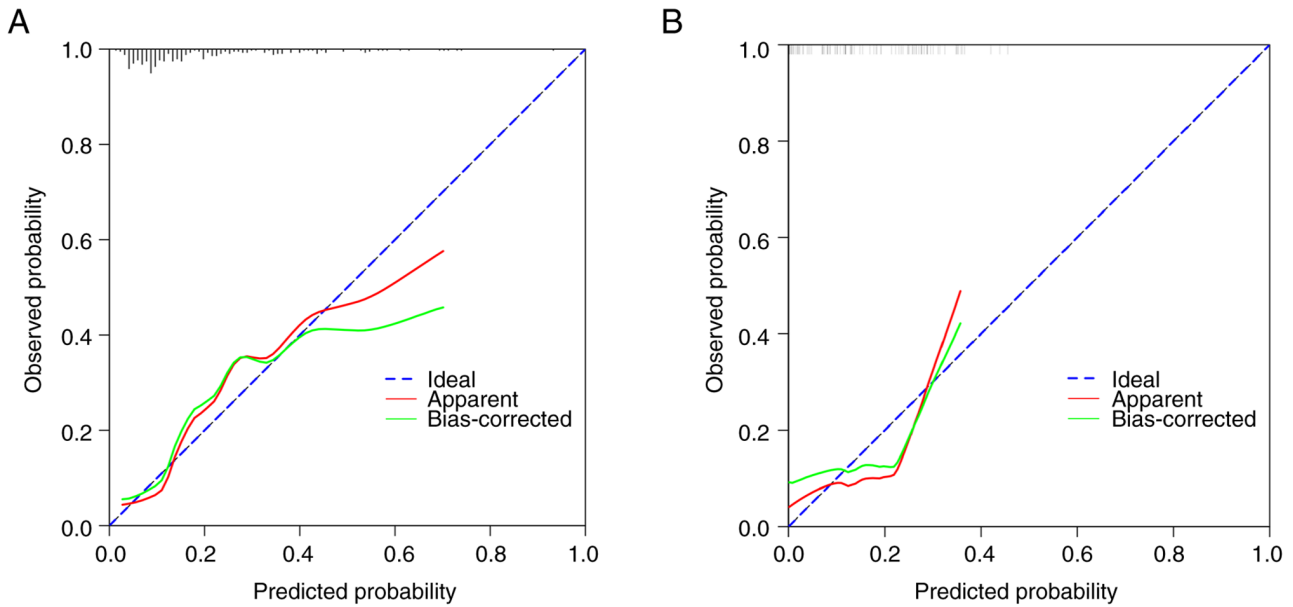


Figure 4. Calibration curves of the (A) training set and (B) internal validation set constructed by the bootstrap method, demonstrating a positive net gain.

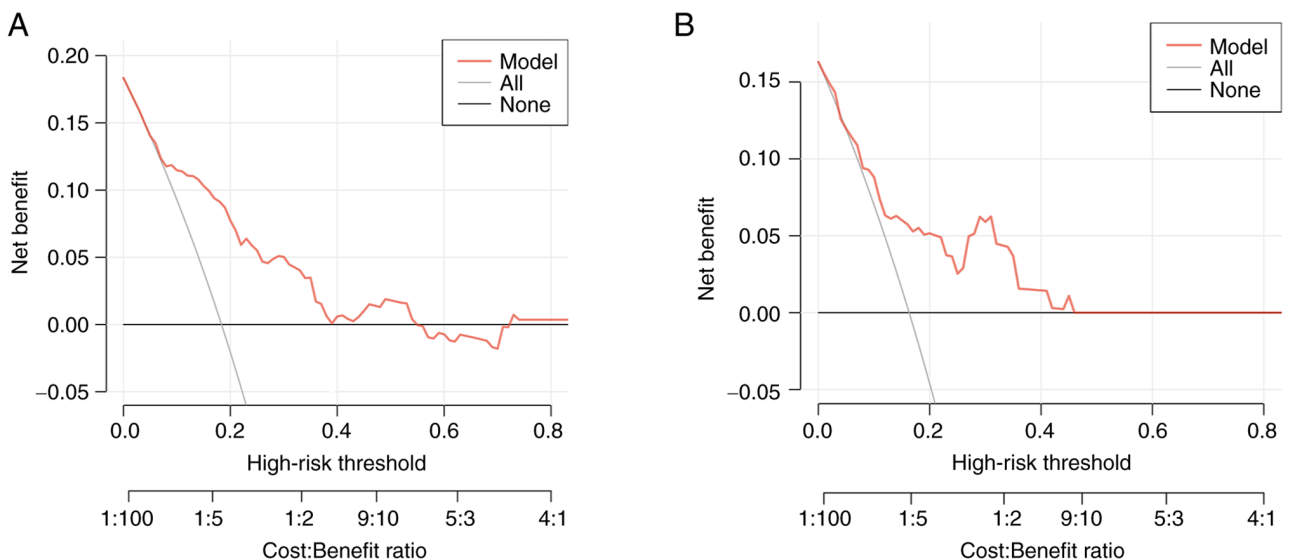


Figure 5. Calibration curves of the nomogram prediction model for the (A) training cohort and (B) internal test cohort, indicating that the data fit well.

and anesthesiologists. The present model encompassed intraoperative variables, thereby enabling anesthesiologists to actively contribute to the management of patients who are considered to be at high risk of developing infections. As a prognostic tool, the dynamic nomogram model could potentially facilitate the process whereby clinicians may quantitatively assess the real-time probability or the risk of infection occurring subsequent to spinal surgery, thereby facilitating the selection of appropriate interventions.

However, the present study also has certain limitations, including its retrospective design, single-center patient population and the need for external validation in diverse populations. Additionally, the model may not comprehensively account for all variables influencing postoperative infections, and the predictive capacity of the model may be impacted by factors beyond the scope of the available dataset. Consequently, future

research endeavors will need to incorporate the performance of prospective studies to gather real-time data, thereby ensuring the continued relevance of the model in the ever-evolving healthcare landscape. Furthermore, a future perspective of the present research is to separate infections of different subtypes and establish corresponding predictive models to more effectively address clinical issues.

In conclusion, dynamic nomograms based on patient sex, diabetes, hypertension, ASA score, BMI, preoperative white blood cells count, preoperative CRP and operative time may have the potential to be a clinically useful predictor of all-cause infection after scoliosis surgery. The predictive model described in the present study could potentially facilitate the real-time visualization of risk factors associated with all-cause infection following surgical procedures in the future.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

RW, JX, QG, YY and MY designed the study. RW, GX and TN contributed to the conception of the study. GL and RW contributed to the analysis of data. JZ, TW, ZC, YW, XT and DS collected the data. YY and MY revised the manuscript. YY and MY confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by the Ethics Committee of the Second Affiliated Hospital of Zhejiang University School of Medicine (approval no. 2022-0968; Hangzhou, China). The requirement for informed consent was waived, since all the patients at the time of surgery provided written consent for their anonymized medical data to be analyzed and published for research purposes.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Yılmaz H, Zateri C, Kusvuran Ozkan A, Kayalar G and Berk H: Prevalence of adolescent idiopathic scoliosis in Turkey: An epidemiological study. *Spine J* 20: 947-955, 2020.
2. Kwan KYH, Koh HY, Blanke KM and Cheung KMC: Complications following surgery for adolescent idiopathic scoliosis over a 13-year period. *Bone Joint J* 102-B: 519-523, 2020.
3. Cognetti D, Keeny HM, Samdani AF, Pahys JM, Hanson DS, Blanke K and Hwang SW: Neuromuscular scoliosis complication rates from 2004 to 2015: A report from the Scoliosis Research Society Morbidity and Mortality database. *Neurosurg Focus* 43: E10, 2017.
4. Patel H, Khoury H, Girgenti D, Welner S and Yu H: Burden of Surgical Site Infections Associated with Select Spine Operations and Involvement of *Staphylococcus aureus*. *Surg Infect (Larchmt)* 18: 461-473, 2017.
5. Casper DS, Zmistowski B, Hollern DA, Hilibrand AS, Vaccaro AR, Schroeder GD and Kepler CK: The effect of post-operative spinal infections on patient mortality. *Spine (Phila Pa 1976)* 43: 223-227, 2018.
6. Heyer JH, Cao NA, Amdur RL and Rao RR: Postoperative complications following orthopedic spine surgery: Is there a difference between men and women?. *Int J Spine Surg* 13: 125-131, 2019.
7. Meyer AC, Eklund H, Hedström M and Modig K: The ASA score predicts infections, cardiovascular complications, and hospital readmissions after hip fracture-A nationwide cohort study. *Osteoporos Int* 32: 2185-2192, 2021.
8. Buja A, Zampieron A, Cavalet S, Chiffi D, Sandonà P, Vinelli A, Baldovin T and Baldo V: An update review on risk factors and scales for prediction of deep sternal wound infections. *Int Wound J* 9: 372-386, 2012.
9. Rodriguez-Merchan EC and Delgado-Martinez AD: Risk factors for periprosthetic joint infection after primary total knee arthroplasty. *J Clin Med* 11: 6128, 2022.
10. Chung AS, Campbell D, Waldrop R and Crandall D: metabolic syndrome and 30-day outcomes in elective lumbar spinal fusion. *Spine (Phila Pa 1976)* 43: 661-666, 2018.
11. Ding JZ, Kong C, Sun XY and Lu SB: Perioperative complications and risk factors in degenerative lumbar scoliosis surgery for patients older than 70 years of age. *Clin Interv Aging* 14: 2195-2203, 2019.
12. TollB J, Samdani AF, Janjua MB, Gandhi S, Pahys JM and Hwang SW: Perioperative complications and risk factors in neuromuscular scoliosis surgery. *J Neurosurg Pediatr* 22: 207-213, 2018.
13. Zhang XN, Sun XY, Hai Y, Meng XL and Wang YS: Incidence and risk factors for multiple medical complications in adult degenerative scoliosis long-level fusion. *J Clin Neurosci* 54: 14-19, 2018.
14. Rudic TN, Althoff AD, Kamalpathy P and Bachmann KR: Surgical site infection after primary spinal fusion surgery for adolescent idiopathic scoliosis: An analysis of risk factors from a nationwide insurance database. *Spine (Phila Pa 1976)* 48: E101-E106, 2023.
15. Menger RP, Kalakoti P, Pugely AJ, Nanda A and Sin A: Adolescent idiopathic scoliosis: Risk factors for complications and the effect of hospital volume on outcomes. *Neurosurg Focus* 43: E3, 2017.
16. Jammer I, Wickboldt N, Sander M, Smith A, Schultz MJ, Pelosi P, Leva B, Rhodes A, Hoeft A, Walder B, *et al*: Standards for definitions and use of outcome measures for clinical effectiveness research in perioperative medicine: European Perioperative Clinical Outcome (EPCO) definitions: A statement from the ESA-ESICM joint taskforce on perioperative outcome measures. *Eur J Anaesthesiol* 32: 88-105, 2015.
17. Peduzzi P, Concato J, Kemper E, Holford TR and Feinstein AR: A simulation study of the number of events per variable in logistic regression analysis. *J Clin Epidemiol* 49: 1373-1379, 1996.
18. Van Calster B, Wynants L, Verbeek JFM, Verbakel JY, Christodoulou E, Vickers AJ, Roobol MJ and Steyerberg EW: Reporting and interpreting decision curve analysis: A guide for investigators. *Eur Urol* 74: 796-804, 2018.
19. Desborough JP: The stress response to trauma and surgery. *Br J Anaesth* 85: 109-117, 2000.
20. Apisarnthanarak A, Jones M, Waterman BM, Carroll CM, Bernardi R and Fraser VJ: Risk factors for spinal surgical-site infections in a community hospital: A case-control study. *Infect Control Hosp Epidemiol* 24: 31-36, 2003.
21. Blanco JF, Díaz A, Melchor FR, da Casa C and Pescador D: Risk factors for periprosthetic joint infection after total knee arthroplasty. *Arch Orthop Trauma Surg* 140: 239-245, 2020.
22. Palestro CJ and Love C: Role of nuclear medicine for diagnosing infection of recently implanted lower extremity arthroplasties. *Semin Nucl Med* 47: 630-638, 2017.
23. Sigmund IK, Dudareva M, Watts D, Morgenstern M, Athanasou NA and McNally MA: Limited diagnostic value of serum inflammatory biomarkers in the diagnosis of fracture-related infections. *Bone Joint J* 102-B: 904-911, 2020.
24. Colborn KL, Zhuang Y, Dyas AR, Henderson WG, Madsen HJ, Bronsert MR, Matheny ME, Lambert-Kerzner A, Myers QWO and Meguid RA: Development and validation of models for detection of postoperative infections using structured electronic health records data and machine learnin]. *Surgery* 173: 464-471, 2023.
25. Aghdassi SJS, Schröder C and Gastmeier P: Gender-related risk factors for surgical site infections. Results from 10 years of surveillance in Germany. *Antimicrob Resist Infect Control* 8: 95, 2019.
26. Soroceanu A, Burton DC, Oren JH, Smith JS, Hostin R, Shaffrey CI, Akbarnia BA, Ames CP, Errico TJ, Bess S, *et al*: Medical complications after adult spinal deformity surgery: Incidence, risk factors, and clinical impact. *Spine (Phila Pa 1976)* 41: 1718-1723, 2016.

27. Tse EY, Cheung WY, Ng KF and Luk KD: Reducing perioperative blood loss and allogeneic blood transfusion in patients undergoing major spine surgery. *J Bone Joint Surg Am* 93: 1268-1277, 2011.
28. Allegranzi B, Bischoff P, de Jonge S, Kubilay NZ, Zayed B, Gomes SM, Abbas M, Atema JJ, Gans S, van Rijen M, *et al.*: New WHO recommendations on preoperative measures for surgical site infection prevention: An evidence-based global perspective. *Lancet Infect Dis* 16: e276-e287, 2016.
29. Onesti MG, Carella S and Scuderi N: Effectiveness of antimicrobial-coated sutures for the prevention of surgical site infection: A review of the literature. *Eur Rev Med Pharmacol Sci* 22: 5729-5739, 2018.
30. Guo Y, Song G, Sun M, Wang J and Wang Y: Prevalence and therapies of antibiotic-resistance in staphylococcus aureus. *Front Cell Infect Microbiol* 10: 107, 2020.
31. Mizan T and Taghipour S: Medical resource allocation planning by integrating machine learning and optimization models. *Artif Intell Med* 134: 102430, 2022.
32. El Sharouni MA, Ahmed T, Varey AHR, Elias SG, Witkamp AJ, Sigurdsson V, Suijkerbuijk KPM, van Diest PJ, Scolyer RA, van Gils CH, *et al.*: Development and validation of nomograms to predict local, regional, and distant recurrence in patients with thin (T1) melanomas. *J Clin Oncol* 39: 1243-1252, 2021.



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