

# Risk prediction model for deep surgical site infection (DSSI) following open reduction and internal fixation of displaced intra-articular calcaneal fracture

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## Abstract

Deep surgical site infection (DSSI) is a serious complication affecting the surgical outcome of displaced intra-articular calcaneal fracture, and a risk prediction model based on the identifiable risk factors will provide great clinical value in prevention and prompt interventions. This study retrospectively identified patients operated for calcaneal fracture between January 2014 and December 2019, with a follow-up  $\geq 1$  year. The data were extracted from electronic medical records, with regard to demographics, comorbidities, injury, surgery and laboratory biomarkers at admission. Univariate and multivariate logistics regression analyses were used to identify the independent factors for DSSI, thereby the risk prediction model was developed. Among 900 patients included, 2.7% developed a DSSI. The multivariate analyses identified five factors independently associated with DSSI, including current smoking (OR, 2.8; 95% confidence interval [CI], 1.3-6.4;  $P = .021$ ), BMI  $\geq 26.4$  kg/m<sup>2</sup> (OR, 3.1; 95% CI, 1.6-8.4;  $P = .003$ ), ASA  $\geq$ II (OR, 1.3; 95% CI, 1.0-5.1;  $P = .043$ ), incision level of II (OR, 3.8; 95% CI, 1.3-12.6;  $P = .018$ ) and NLR  $\geq 6.4$  (OR, 3.2; 95% CI, 1.3-7.5;  $P = .008$ ). A score of 14 as the optimal cut-off value was corresponding to sensitivity of 0.542 and specificity of 0.872 (area, 0.766;  $P < .001$ );  $\geq 14$  was associated with 8.1-times increased risk of DSSI; a score of 7 was corresponding sensitivity of 100% and 10 corresponding to sensitivity of 0.875. The risk prediction model exhibited excellent performance in distinguishing the risk of DSSI and could be considered in practice for improvement of wound management, but its validity requires to be verified by better-design studies.

## KEYWORDS

calcaneal fracture, deep surgical site infection, multivariate analysis, receiver operating characteristic (ROC), risk prediction model

## Key messages

- the incidence rate of DSSI following open reduction and internal fixation of displaced calcaneal fractures is 2.7%

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- a risk prediction model is constructed based on five identified factors and exhibits the excellent performance
- patients with a score of  $\geq 14$  had a very high risk of DSSI and should be considered as high-risk population
- a score of 7 or 10 had a high sensitivity, ranging from 87.5% to 100%, hence providing value in evaluating the risk of DSSI

## 1 | INTRODUCTION

Displaced intra-articular calcaneal fracture (DIACF) is prevalent in department of orthopaedic trauma, involving approximately 2% of overall fractures and approximately 30% of foot and ankle fractures.<sup>1,2</sup> By far, open reduction and internal fixation (ORIF) remains the standard modality of operative treatment, but is not without drawbacks. The first concern was the high rate of wound-related complications, especially the deep surgical site infection (DSSI), which affected 2.9% to 15.4% of surgically treated patients.<sup>3-5</sup> DSSI was associated with substantial health care burden from repeated wound debridement, revision or implant removal, and social consequences due to the occasional amputation or sequela of limb dysfunction.<sup>6,7</sup>

In practice, the importance of preventing DSSI cannot be overemphasised. This is especially true for high-risk patients, who, in other word, may gain most benefits from targeted preventive interventions. More importantly, identification of the high-risk patients via the identified factors and accordingly targeting them with interventions is the most cost-effective method. In fact, in clinical investigations, it is the consistent aim to keep identifying risk factors (especially the modifiable or controllable factors) for the development of a DSSI.<sup>4,8-11</sup> However, due to heterogeneity in institutional policy (operating room availability, operation schedule reasonability, prophylactic antibiotic use, wound care), surgeon preference (wound drainage or type of prophylactic antibiotics), patients' conditions (comorbidities, obesity, smoking, non-compliance) and surgery-related factors (inadequate surgical skills, surgical approach), the results available from these studies might not be so generalizable. In addition, the relatively small sample size and no inclusion of so many variables for adjustment made them difficult to obtain conclusive results, and possibly there remain some factors that have never been investigated or noticed.

In this study, we used the large sample of calcaneal fracture surgically treated by ORIF in a tertiary referral institution to address our aims: (1) to investigate the incidence rates of DSSI; (2) to identify the factors independently associated with DSSI; and (3) on basis of these factors, if any, to form a risk model for predicting the DSSI and evaluate its predictive power.

## 2 | METHODS

### 2.1 | Inclusion and exclusion criteria

This study retrospectively identified patients aged 18 years or older who underwent surgical treatment of acute closed calcaneal fractures by ORIF in our institution between January 2014 and December 2019, with postoperative follow-up period of a minimum of 12 months. Patients with complete follow-up data were deemed to be eligible for inclusion. The exclusion criteria were age less than 18 years, open calcaneal fracture, bilateral calcaneal fracture, pathological fractures, old fractures ( $> 21$  days from initial injury), multiple fractures, polytrauma, treatments rather than ORIF (conservative, closed reduction, percutaneous fixation, external fixation et al), presence of infections or signs before index fracture operation, wound issues other than DSSIs (superficial infection, wound edge necrosis, erythema), missing data for any variable of interest or incomplete follow-up data. This study was approved by the local ethics committee, which waived the need for informed consent.

### 2.2 | Perioperative management

For ORIF procedure via extended lateral approach or sinus tarsi approach, 1 to 2 g of cefazolin on the basis of weight was administered to all patients within 30 minutes before skin incision, and in case of procedure predicted to last over 3 hours, another dose was given. Within 24 hours after wound closure, prophylactic use of 1 to 2 g of cefazolin was routinely given, and for patients with high-risk infection, the period could be appropriately extended. Pneumatic tourniquets, bone-grafting and postoperative drainage use were left to the discretion of the treating surgeon. Postoperatively, all patients were instructed to follow the same protocol on wound care and physical exercises.

### 2.3 | Data collection

Two investigators (K.L and T.M) independently extracted the data from the inpatient electronic medical records

and documented them using the EpiData software (version 3.1, The EpiData Association, Odense, Denmark), and any discrepancies were resolved by consensus. Then, these data were exported into the Excel worksheet (Office version 2016) for the purpose of statistical description and analysis.

The collected data were demographics (age, sex, body weight, height, occupation, education level), lifestyles (current smoking status, alcohol consumption), comorbidities or conditions (hypertension, diabetes mellitus, chronic heart disease), injury-related (injury mechanism and fracture type based on Sander' classification), surgery-related (time from injury to surgery, surgical approach, surgical duration, blood loss, allogeneic blood transfusion, anaesthesia type, American Society of Anesthesiologists [ASA] grade, bone-grafting, postoperative drainage use), and laboratory indexes measured at admission (count of white blood cell, neutrophil, lymphocyte, red blood cell and platelet, level of plasma albumin, total protein, haemoglobin and fasting blood glucose). We also calculated the values of ratio of neutrophil to lymphocyte and platelet to lymphocyte, and investigated whether they are in relation to the development of DSSI, both of which have demonstrated to be associated with multiple adverse outcomes (venous thromboembolism, infection, mortality) across a wide range of specialties (trauma, cancer, cardia-cerebrovascular disease).<sup>8,10,12-14</sup>

Occupation was categorised as retirement, office work, manual work and others (students, unemployment). Based on attainment of years, education level was categorised as illiteracy, <6, 6 to 12 and >12 years. Body mass index was calculated by dividing the square of height in metre by the weight in kilogram, and was divided into non-obesity (<28 kg/m<sup>2</sup>) and obesity (≥28 kg/m<sup>2</sup>) based on the criteria fit for Chinese people, and further was dichotomised according to the cut-off value determined by algorithm. Current smoking or alcohol consumption was defined as patients' self-reported smoking activity or drinking of wine, beer or any other alcoholic beverage alcohol within 12 months of the index operation. Considering the clinical relevance for explorable analysis, the laboratory indexes were divided into two or three categories, as appropriate. Injury mechanism was dichotomised as high-impact trauma (e.g. traffic accidents, fall from height ≥1 m, and other violent injuries) and low-to medium-impact trauma (fall from height <1 m or standing height).

## 2.4 | Definition and confirmation of DSSI

Definition of DSSI is based on the criteria issued by the US Centers for Disease Control and Prevention, referring

to an infection directly related to the wound and involving the tissues surpassing the deep fascia. DSSI was identified and confirmed by checking the descriptions in the electronic medical records on the basis of at least one of the following incision-related signs: pus discharging; dehiscence or separation; various examinations or medication prescriptions and dispensations providing evidence for SSI; and debridement or/and removal of implant performed. Of note, for superficial SSI or other minor wound issues such as wound edge necrosis or erythema that resolved by wound care or oral antibiotics alone, we did not include them in the analysis for the purpose of ruling out potential confounding effects.

For those who were readmitted within the 1 year of index operation, we used their national identification card number rather than the inpatient record number to confirm the potential DSSI cases, because only the former was unique for one person.

## 2.5 | Statistical analysis

The continuous variables were presented as mean ± standard deviation (SD), using Kolmogorov-Smirnov test and Levene's test to evaluate the normality status and homogeneity of variances, respectively. Student *t*-test or Mann-Whitney *U*-test was used to detect the difference between groups, as appropriate. Categorical data were presented as a number with a percentage and compared by Chi-square test or Fisher exact test, as appropriate.

Receiver operating characteristic (ROC) curve was constructed to determine the optimal cut-off value for age, BMI, NLR and PLR, when sensitivity +1-specificity (namely, Youden index) was maximised. Based on the cut-off values (BMI, 26.4 kg/m<sup>2</sup>; NLR, 6.4; PLR, 150; age, 45 years), they were dichotomised and compared between groups in univariate analyses. Variables tested with *P* < .10 were further entered into the multivariate logistics regression model to determine their independent effects on development of DSSI, using stepwise backward method. The goodness-of-fit of the final model was evaluated using Hosmer-Lemeshow (H-L) test, with *P* value >.05 considered as the acceptable result. Variables with statistical level of *P* < .10 were retained in the final model. Odds ratio (OR) and its 95% confidential interval indicated the magnitude of association effect.

For each independent variable, a scoring point (integer value, derived from the rounded-up ORs) was assigned; therefore, the potential assigned point was zero, or otherwise the rounded-up OR value. For any patient, the total score was calculated by totalling the scores from all independent variables existing for him/her. Again, ROC curve was made for determining the rate of DSSI

for every possible value for the total score (independent factor), while the optimal cut-off value was calculated with the rate of DSSI as the dependent factor. The validity of the cut-off value was evaluated by means of comparing the area under the ROC curve (AUC), as previously described in detail.<sup>15</sup>

The statistical significance was set as  $P < .05$  and all the analyses were performed using SPSS24.0 (IBM Corporation, New York, USA).

### 3 | RESULTS

Within the study period, 1407 calcaneal fractures were retrieved and 507 patients were excluded based on our rigorous criteria, leaving 900 for data analysis (details presented in Figure 1). Among them, male patients predominated overwhelmingly (92.8%, 835/900). The age averaged  $41.8 \pm 11.8$  years at injury, with  $\leq 45$  years in 62.5% of patients. These ORIF procedures were performed by 32 surgeons. Approximately 40% of patients were operated within 7 days, and 93.8% within 14 days after injury. The predominant surgical approach was extended lateral approach in 71.0% of patients.

DSSI was developed in 24 patients, representing an accumulated incidence of 2.7%. The median interval was 27 days (range 6-206 days) between operation DSSI and 70.8% (17/24) occurred within 3 months.

Compared with those without developing a DSSI, patients with a DSSI had a significantly prolonged hospital stay ( $24.1 \pm 24.6$  vs  $16.1 \pm 8.5$ ,  $P = .001$ ). Twenty patients received reoperation that was debridement alone in eight patients, implant removal in five patients, flap repair procedure in two patients and others in five patients. No amputation was performed. The average number of surgical procedures needed for control of infection was 1.8, 2 or more in three-fifths (12/20) of the patients (Table 1).

The optimal cut-off values were determined for NLR (6.4), PLR (150), BMI ( $26.4 \text{ kg/m}^2$ ) and age (45 years). (Figure 2) Compared with the non-DSSI group, patients with a DSSI had a significantly higher BMI ( $26.8 \pm 3.6$  vs  $25.1 \pm 3.5$ ,  $P = .023$ ) and a higher proportion of BMI  $\geq 26.4 \text{ kg/m}^2$  ( $P = .001$ ) and  $\geq 28.0$  ( $P = .039$ ), were more likely current smokers (33.3% vs 15.4%), and had an incision of greater level (II, 12.5% vs 3.5%), TP level ( $67.8 \pm 5.7$  vs  $65.0 \pm 6.1$ ,  $P = .024$ ), albumin level ( $44.4 \pm 2.9$  vs  $41.2 \pm 5.1$ ,

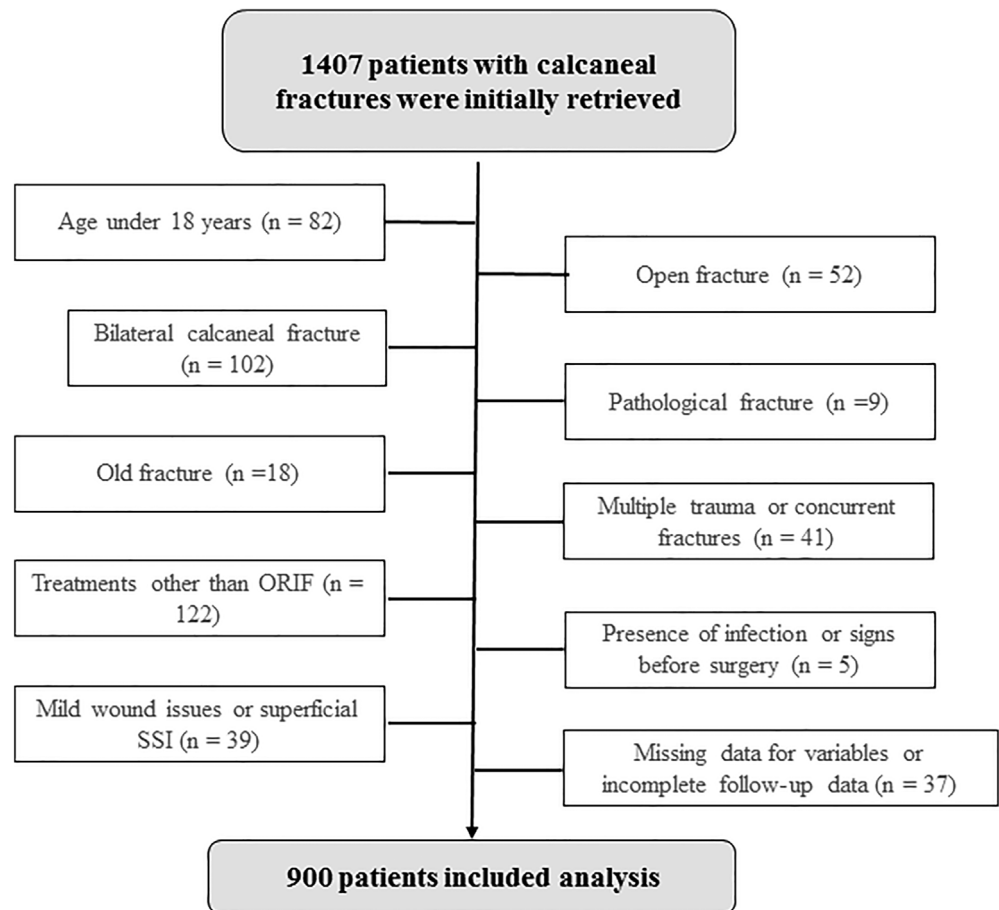


FIGURE 1 The flow chart showing the screening of patients meeting the criteria for inclusion for data analysis

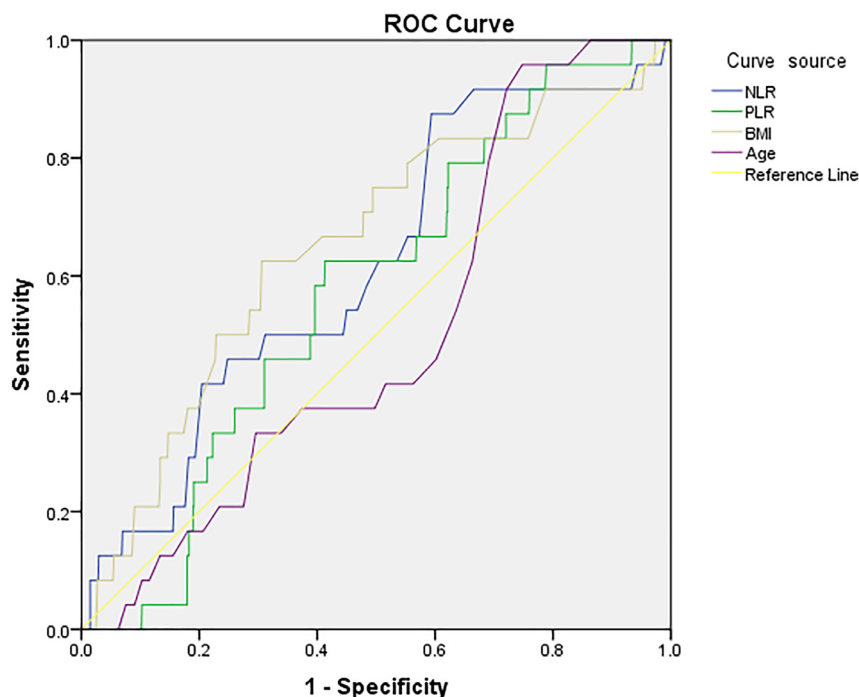
**TABLE 1** Comparisons between SSI and non-SSI group in terms of demographics, patient, injury surgery variables and the biomarkers measured at admission

Variable	Non-SSI group (n = 876)	SSI group (n = 24)	P value
Sex (male)	812 (92.7)	23 (95.8)	.558
Age (years)	41.9 ± 11.2	41.5 ± 8.7	.863
≤45	518 (59.1)	15 (62.5)	.740
BMI (kg/m <sup>2</sup> )	25.1 ± 3.5	26.8 ± 3.6	.023
≥26.4 (vs <26.4)	273 (31.2)	15 (62.5)	.001
≥28.0 (vs <28.0)	150 (17.1)	8 (33.3)	.039
Occupation			.857
Office work	109 (12.4)	2 (7.7)	
Labouring	448 (51.3)	15 (62.5)	
Retirement	67 (7.6)	2 (7.7)	
Manual work	150 (17.2)	3 (12.5)	
Others	102 (11.7)	4 (15.4)	
Attainment of education (years)			.570
Illiteracy	57 (6.5)	2 (8.3)	
<6	227 (25.9)	9 (37.5)	
6-11.9	482 (55.0)	11 (45.8)	
≥12	110 (12.6)	2 (8.3)	
Current smoking	135 (15.4)	8 (33.3)	.018
Current drinking	278 (31.7)	9 (37.5)	.550
Hypertension	76 (8.7)	3 (12.5)	.514
Diabetes mellitus	42 (4.8)	2 (8.3)	.754
Heart or cardiovascular disease	23 (2.4)	1 (4.2)	1.000
History of any surgery	32 (3.7)	2 (8.3)	.235
Injury mechanism (high-impact trauma)	625 (71.3)	21 (87.5)	.107
Fracture types (Sanders grades)			.953
II	445 (50.8)	14 (56.5)	
III	288 (32.9)	7 (30.4)	
IV	143 (16.3)	3 (13.0)	
Time from injury to operation (day)	8.0 ± 4.6	8.0 ± 4.9	.990
<7	352 (40.2)	10 (41.7)	.413
7-10	337 (38.5)	6 (25.0)	
11-14	128 (14.6)	5 (20.8)	
>14	59 (6.7)	3 (12.5)	
Length of hospital stay	16.1 ± 8.5	24.1 ± 24.6	.001
Operative time	126.7 ± 70.8	134.2 ± 79.2	.610
Intraoperative blood loss	167.9 ± 186.9	172.6 ± 113.9	.905
Incision level			.023
I	845 (96.5)	21 (87.5)	
II	31 (3.5)	3 (12.5)	
ASA grade			.089
I	153 (17.5)	1 (4.2)	
II or greater	723 (82.5)	23 (95.8)	
Anaesthesia mode			.848
Regional (epidural/spinal)	679 (77.5)	19 (79.2)	

TABLE 1 (Continued)

Variable	Non-SSI group (n = 876)	SSI group (n = 24)	P value
General	197 (22.5)	5 (20.8)	
Surgical approach			.371
Tarsal sinus approach	256 (29.2)	5 (20.8)	
Extended lateral approach	620 (70.8)	19 (79.2)	
Bone-grafting			.454
Yes	72 (8.2)	3 (12.5)	
No	804 (91.8)	21 (87.5)	
Drainage use	353 (40.3)	7 (29.2)	.272
Allogeneic blood transfusion	69 (7.9)	4 (16.7)	.120
TP (g/L)	65.0 ± 6.1	67.8 ± 5.7	.024
<60 g/L	165 (18.8)	1 (4.2)	.068
Albumin (g/L)	41.2 ± 5.1	44.4 ± 2.9	.002
<35 g/L	95 (10.8)	0	.171
HCRP (mg/L)	30 ± 33.6	26.2 ± 44.8	.603
>8 mg/L	604 (68.9)	13 (54.2)	.124
LDH (U/L)	235.7 ± 117.7	223.2 ± 53.3	.605
>250 U/L	292 (33.3)	10 (41.7)	.394
Sodium concentration (mmol/L)	139.0 ± 3.2	139.9 ± 2.5	.167
<135 mmol/L	202 (23.1)	1 (4.2)	.029
FBG (mmol/L)	5.8 ± 1.5	5.6 ± 1.2	.663
≥6.1 mmol/L	192 (21.9)	6 (25.0)	.719
WBC (×10 <sup>9</sup> /L)	8.9 ± 2.6	10.1 ± 3.3	.036
>10 × 10 <sup>9</sup> /L	331 (37.8)	14 (58.3)	.041
Neutrophil (10 <sup>9</sup> /L)	6.5 ± 2.4	7.8 ± 3.3	.011
>6.3 × 10 <sup>9</sup> /L	413 (47.1)	15 (62.5)	.137
Lymphocyte (×10 <sup>9</sup> /L)	1.6 ± 0.6	1.5 ± 0.5	.444
<1.1 × 10 <sup>9</sup> /L	162 (18.5)	6 (25.0)	.420
platelet (×10 <sup>9</sup> /L)	228.3 ± 79.7	229.1 ± 62.3	.960
>300 × 10 <sup>9</sup> /L	124 (14.2)	5 (20.8)	.357
NLR	4.8 ± 3.1	6.0 ± 3.8	.044
<6.4	696 (79.5)	14 (58.3)	.012
≥6.4	180 (20.5)	10 (41.7)	
PLR	160.5 ± 83.9	162.1 ± 48.2	.927
<150	518 (59.1)	10 (41.7)	.086
≥150	358 (40.9)	14 (58.3)	
RBC (×10 <sup>12</sup> /L)	4.2 ± 0.6	4.5 ± 0.5	.089
<Lower limit	168 (19.2)	2 (8.3)	.181
Haemoglobin (g/L)	134.5 ± 17.3	138.5 ± 14.4	.256
<Lower limit	117 (13.4)	2 (8.3)	.474
HCT (percentage)	39.7 ± 5.3	40.9 ± 4.1	.280
<Lower limit	120 (13.7)	4 (2.7)	.677

Note: Data presentation, mean ± SD (standard deviation) or number (percentage); BMI, body mass index; ASA, American Society of Anesthesiologists; TP, total protein; HCRP, hyper-sensitive C-reaction protein; HDH, lactate dehydrogenase; WBC, white blood cell; FBG, fasting blood glucose; NLR, neutrophil/lymphocyte ratio; PLR, platelet/lymphocyte ratio; RBC, red blood cell, reference range: female, 3.5 to 5.0 × 10<sup>12</sup>/L; male, 4.0 to 5.5 × 10<sup>12</sup>/L. Haemoglobin, reference range: Female, 110 to 150 g/L; male, 120 to 160 g/L. HCT, haematocrit, reference range: female, 35% to 45%; male, 40% to 50%.



**FIGURE 2** ROC curve for determination of the optimal cut-off values for NLR (6.4), PLR (150), BMI (26.4 kg/m<sup>2</sup>) and age (45 years). Horizontal axis represents the 1-specificity and vertical axis indicates the sensitivity of each variable in predicting development of DSSI. The lines in different colours represent the different variables. The area under the curve (AUC) represents the ability to discriminate the DSSI cases

**TABLE 2** Assigned score for each variable based on their independent association of magnitude with DSSI

Variable	Association of magnitude (OR and 95% CI)			Assigned score
	OR	95% CI	P	
Current smoking	2.8	1.3-6.4	.021	3
BMI $\geq 26.4$ kg/m <sup>2</sup>	3.1	1.6-8.4	.003	3
ASA ( $\geq$ II vs I)	1.3	1.0-5.1	.043	1
Incision level (II vs I)	3.8	1.3-12.6	.018	4
NLR ( $\geq 6.4$ vs $< 6.4$ )	3.2	1.3-7.5	.008	3

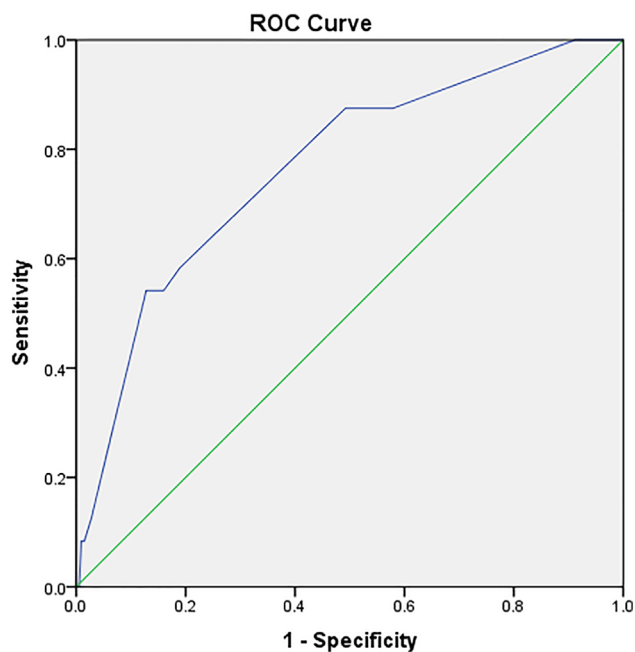
Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; CI, confidential interval; DSSI, deep surgical site infection; NLR, neutrophil/lymphocyte ratio; OR, odd ratio.

$P = .002$ ), WBC count ( $10.1 \pm 3.3$  vs  $8.9 \pm 2.610 \times 10^9/L$ ,  $P = .036$ ) and proportion of WBC  $> 10 \times 10^9/L$  (58.3% vs 37.8%,  $P = .041$ ), neutrophil count ( $10.1 \pm 3.3$  vs  $8.9 \pm 2.6 \times 10^9/L$ ,  $P = .011$ ), NLR value ( $6.0 \pm 3.8$  vs  $4.8 \pm 3.1$ ,  $P = .044$ ) and higher proportion of NLR  $> 6.4$  (41.7% vs 20.5%,  $P = .012$ ). For other variables, no significant differences were found.

Entered in the multivariate logistics regression model were the above significant variables and additionally those with  $P < .10$  who were ASA grade, TP and PLR in dichotomised category, and RBC in continuous variable. The final results showed that current smoking (OR, 2.8;  $P = .021$ ), BMI  $\geq 26.4$  kg/m<sup>2</sup> (OR, 3.1;  $P = .003$ ), ASA  $\geq$ II (OR, 1.3;  $P = .043$ ), incision level of II (OR, 3.8;  $P = .018$ ) and NLR  $\geq 6.4$  (OR, 3.2;  $P = .008$ ) were independently associated with the development of DSSI. For each variable, the corresponding score was assigned (Table 2). Hosmer-

Lemeshow test demonstrated an acceptable goodness-of-fit of the model ( $X^2 = 4.118$ ,  $P = .306$ ).

Based on our predefined algorithm, the average score for one patient was 10 (median, 11; range 4-21). The ROC results showed the AUC was 0.766 (95% CI, 0.670-0.863;  $P < .001$ ) and a score of 14 was the optimal cut-off value, corresponding to sensitivity of 0.542 and specificity of 0.872. One hundred and twenty-five patients had a score of  $\geq 14$  among whom 13 (10.4%) developed a DSSI; while 775 patients had a score of  $< 14$ , and 11 (0.13%) developed a DSSI. This suggested a score of  $\geq 14$  was associated with 8.1-times increased risk of DSSI (Chi-square test, 95% CI, 3.5-18.4;  $P < .001$ ). We also investigated another 2 seconds optimal cut-off values for sensitivity of most clinical relevance, which had a score of 7 (sensitivity, 100%) and a score of 10 (sensitivity, 0.875) (Figure 3).



**FIGURE 3** ROC curve for the summed score to determine its optimal cut-off for distinguishing the DSSIs from non-DSSIs. The AUC was 0.766 (95% CI, 0.670-0.863;  $P < .001$ ) and a score of 14 was the optimal cut-off value, corresponding to sensitivity of 0.542 and specificity of 0.872. A score of 7 as cut-off value is corresponding to the sensitivity of 100%, and of 10 responding to sensitivity of 0.875. Horizontal axis represents the 1-specificity and vertical axis indicates the sensitivity of each variable in predicting the development of DSSI

## 4 | DISCUSSION

DSSI in the field of orthopaedic trauma surgery has been consistently a focus in both clinical practice and scientific research. In this study, we identified several important factors, thereby forming a valuable risk prediction model. The model showed that a score of  $\geq 10$  should alert the risk of DSSI (sensitivity, 0.875), a score of 14 or more is strongly predictive of development of DSSI (OR, 8.1), and a score of  $< 7$  almost could rule out the possibility of DSSI.

Compared with the high variable rates of SSI (5.0%-25.0%)<sup>11,16,17</sup> or DSSI (2.9%-15.4%)<sup>3-5</sup> in the literature, we reported a relatively lower incidence rate of 2.7%. This was mainly decided by the predefined rigorous inclusion and exclusion criteria and the narrower definition of DSSI. Some injuries or medical conditions at high risk of DSSI had been excluded, including open fracture, multiple trauma or bilateral calcaneal fractures.<sup>6,11</sup> The rapid improvement in operative techniques, implant material property, standardisation of antibiotics prophylaxis and wound care in orthopaedic trauma during the past 30 years has contributed to decreasing the SSIs overall.<sup>18</sup>

Another reason might be that we only inquired index hospitalisation or re-hospitalisation medical records for confirmation of DSSIs, leaving those with DSSI treated in other institutions excluded acquiescently.

Identification of risk factors and accordingly targeting prophylactic measures do help with effective perioperative management of surgical wound. In the present study, we used a thoroughly selected population with a huge amount of sample to address the risk factors of DSSI following calcaneal fracture. It is of note, four out of five factors identified had been repeatedly investigated and their role was well-established across studies with different levels of evidence.<sup>4,8-10,19</sup> The only difference among them might be the determination of cut-off values of BMI, for which we used both the traditional value (28.0 g/m<sup>2</sup>, for definition of obesity for Chinese people) and the current value of 26.4 kg/m<sup>2</sup> to make a dichotomization. As a result, the latter demonstrated to be more sensitive in prediction of DSSI ( $P < .001$ ). We inferred that the younger age (mean, 41.8 years) and slimmer figure (BMI, mean, 25.1 kg/m<sup>2</sup>) in this selected group contributed to this discrepancy.

As a novel indicator, NLR was firstly identified as an independent factor for predicting the development of DSSI in this study, which could be explained by it being an indicator of magnitude of body's systemic inflammatory response<sup>20</sup> and further the cumulative effects of persistent acute inflammatory response after surgery.<sup>13</sup> Our finding complemented the recent reports regarding the prediction role in adverse results following orthopaedic surgeries. For example, NLR demonstrated to be capable of predicting the mortality and cardiovascular complications after hip fracture,<sup>13</sup> the risk of venous thromboembolic events (VTE) after total knee arthroplasty,<sup>12</sup> the degree of inflammatory response/infection and onset of myocardial injury in orthogeriatric patients.<sup>21</sup> In addition, in non-orthopaedics specialties, NLR has also demonstrated its relation with adverse outcomes, onset of acute or chronic complications, or poor conditions.<sup>14,22,23</sup> In this study, patients with NLR  $\geq 6.4$  are highly vulnerable to the development of a DSSI (OR, 3.2), to whom specific attention should be paid to control those combined modifiable factors (smoking, dose of prophylactic antibiotics).

By far as we know, this is the first report of development of a risk model for predicting DSSI specifically following calcaneal fracture. Its feasibility in clinical application and potential advantages were predictable. First, this model was formed based on four well-established risk factors in the literature and one novel biomarker. Particularly, the latter was derived from the blood routine examination results (neutrophil and lymphocyte count), both of which are readily available and hence without adding any extra cost for patients. Second,



this model uses the score of 10 (with a sensitive of 0.875) to stratify patients into high-risk and low-risk categories, which was conducive to targeted prevention of DSSIs. It is of particular note that a score of  $\geq 14$  was identified to be associated with 8.1-times increased risk of DSSI, and patients in this category should be paid more attention to and if conditional, specifically protocolised surveillance could be developed. Third, all the DSSI cases occurred in patients with a score of  $\geq 7$ , and hence a score of  $< 7$  contributes to almost completely rule out the possibility of DSSI, possibly avoiding the generalised coverage of infection control resources.

Several limitations to this study should be mentioned. First, the retrospective nature of this study limited the accuracy and precision in data collection, although the double-entry might partly offset this bias. For some variables (smoking) volume and frequency might be particularly important parameters in infection complications, but detailed data were not available. Second, the volume of surgeon might affect the results, because surgical treatment of calcaneal fracture needs a learning curve, especially for tarsal sinus.<sup>19</sup> As plenty of surgeons perform operations, the sample size of operations for each surgeon in 1 year is too small to obtain effective statistical analyses. Third, as with every multivariate analysis, there remain the unknown or unmeasured confounders to bias the results, despite numerous variables included in this study. Fourth, the single-centre setting may limit the generalizability of our findings, because patients admitted or transferred commonly have severe injury or poorer comorbid conditions. Fifth, as we discussed previously, we could not identify those who had developed a DSSI but sought treatment in other institutions, resulting in underestimation of such key complication.

In summary, the incidence rate of DSSI following ORIF of calcaneal fractures was 2.7% and five independent factors were identified, most of which were well-established in the literature. The risk prediction model exhibited its excellent capability in distinguishing those with high- and low-risk of DSSI, with different but appropriate cut-off values. Our findings should be looked upon in the context of specific or general limitations, and the validity of the risk prediction model should be verified by prospective and multicentre studies of a larger sample size.

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#### CONFLICT OF INTEREST

The author(s) declared no potential conflict of interest with respect to the research, authorship, and/or

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#### AUTHOR CONTRIBUTIONS

Kaosheng Lu designed the study; Kaosheng Lu, Tiaoxiao Ma followed up the patients and collected the data. Chunyan Yang and Haibo Liu analysed and interpreted the data; Qu Q searched the relevant literature; Kaosheng Lu wrote the manuscript and all the authors approved the final version of the manuscript.

#### ETHICAL APPROVAL

Permission was obtained from the Institutional Review Board.

#### DATA AVAILABILITY STATEMENT

Peer review of empirical data will be conducted to confirm that the data reproduce the analytic results reported in the paper.

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