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Construction and validation of a nomogram model for predicting the risk of recurrence in patients with lower extremity arteriosclerosis obliterans after surgical intervention

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Abstract

Objective To explore and analyze the risk factors for recurrence in patients with lower extremity arteriosclerosis obliterans (ASO) after surgical intervention and to construct and validate a nomogram prediction model.

Methods A total of 270 patients with ASO treated at our hospital were retrospectively selected as study subjects and divided into a training cohort (189 cases) and a validation cohort (81 cases) based on a 7:3 ratio. Patients in the training cohort were further divided into recurrence and non-recurrence groups based on whether they experienced recurrence within two years post-surgery. Univariate and multivariate logistic regression analyses were employed to identify independent risk factors for postoperative recurrence, which were then used to construct a predictive model and generate a nomogram.

Results Of the 270 patients with ASO included in the study, the training cohort consisted of 189 patients, with 76 (40.21%) in the recurrence group and 113 (59.79%) in the non-recurrence group. The validation cohort consisted of 81 patients, with 32 (39.51%) in the recurrence group and 49 (60.49%) in the non-recurrence group. Univariate analysis in the training cohort revealed significant differences in age, body mass index (BMI), diabetes, hypertension, lesion location classification, use of antiplatelet drugs, triglycerides, fibrinogen (FIB), and di-dimer (D-D) ($P < 0.05$, respectively). Multivariate logistic regression analysis indicated that age ≥ 60 years, BMI ≥ 24 kg/m^2, diabetes, hypertension, discontinuation of antiplatelet therapy, FIB, and D-D were independent risk factors for recurrence after surgical intervention in patients with lower extremity ASO (OR = 2.471, 1.625, 4.568, 2.678, 5.974, 2.073 and 3.067; $P < 0.05$, respectively). When the training and validation cohorts were tested in the established nomogram model, the area under the curve (AUC) of the model was 0.832 (95% CI: 0.765–0.919) in the training cohort and 0.858 (95% CI: 0.745–0.964) in the validation cohort. Calibration curves indicated high consistency between the predicted and actual

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outcomes in both groups, suggesting good predictive accuracy of the model. Decision curve analysis showed that using this model significantly increased net clinical benefit for patients.

Conclusion The nomogram model constructed for predicting the risk of recurrence in patients with lower extremity ASO after surgical intervention demonstrates good predictive and discriminative abilities, offering valuable guidance for clinical screening of high-risk populations.

Keywords Lower extremity arteriosclerosis obliterans, Angioplasty, Recurrence, Nomogram, Predictive model

Lower extremity arteriosclerosis obliterans (ASO) is a common vascular disease primarily caused by the formation of atherosclerotic plaques, leading to vascular stenosis and occlusion, which in turn results in chronic ischemia of the limbs [1, 2]. Patients often exhibit symptoms such as coldness, numbness, and pain in the affected limb, severely impacting their quality of life [2]. Intervention for ASO involves puncturing the femoral artery, guiding a wire to the occluded vessel, and restoring blood supply through balloon dilation [3] or stent implantation [4]. However, patients still face a high risk of recurrence after the procedure, with the recurrence rate reportedly as high as 50% within one year [5, 6]. Therefore, predicting and assessing the risk of recurrence after surgical intervention in patients with lower extremity ASO is of great significance for developing effective preventive measures and improving patient outcomes [7]. A nomogram, a quantitative analysis tool, visually displays the functional relationship between multiple variables and estimates the probability of an event occurring through non-intersecting line segments. It has been widely applied in cancer prognosis and disease risk assessment [8]. Currently, no study has conducted a multifactorial analysis of preoperative, intraoperative, and postoperative clinical indicators of patients with ASO to establish an accurate predictive model. This study aims to construct a nomogram model for predicting the risk of recurrence in patients with lower extremity ASO after surgical intervention, validate the model, and explore its clinical value in improving the efficacy of clinical interventions.

Materials and methods

Clinical data

Patients with ASO who were treated at our hospital from Jan 2020 to Jan 2024 were retrospectively selected as study subjects. Inclusion criteria were as follows: (1) Patients with a confirmed diagnosis of ASO [9] based on medical history(The formation of atherosclerotic plaques in lower limbs leads to stenosis and occlusion of lower limb arteries, which leads to chronic limb ischemia), physical examination(Decreased skin temperature, pallor or cyanosis of the affected limb; Decreased or disappeared arterial pulsation; Limb motor dysfunction, pain caused by changes in limb position; Ulcer or gangrene; Ankle-brachial index(ABI) < 1.0 on the affected side), and imaging findings(The superficial femoral artery stenosis > 50% as indicated by Duplex ultrasound and computed tomography angiography (CTA)); (2) Patients who underwent surgical intervention by the same treatment team. Exclusion criteria included: (1) Patients with concurrent active arteritis; (2) Patients with incomplete laboratory results, imaging data, pathological findings, or follow-up records; (3) Patients with poor compliance who did not cooperate with treatment. The study protocol was approved by the hospital's ethics committee. All patients' medical records and follow-up data were kept confidential by designated personnel.

Methods

The intervention strategy was based on ASO guidelines [10, 11]. Preoperative CTA was performed, and the treatment plan was determined according to the Trans-Atlantic Inter-Society Consensus (TASC) classification. For TASC A–B lesions, endovascular therapy was the first choice; if balloon angioplasty was unsatisfactory, stenting was performed. For TASC C–D lesions, endovascular therapy was attempted, and if unsuccessful, the patient was referred for surgery. Patients were followed up for one year postoperatively. According to the ASO diagnosis and treatment guidelines, patients were divided into a recurrence group and a non-recurrence group based on whether recurrence occurred within one year. Recurrence was defined as stenosis or occlusion > 50% in the target vessel as indicated by Doppler ultrasound or CTA after the intervention.

The pre-treatment clinical, pathological, and laboratory characteristics analyzed in this study included age(60 years old as the boundary of old age), gender, body mass index (BMI, 24 kg/m^2 as the boundary of obese people), smoking history, alcohol consumption history, previous medical history (Whether there is coronary heart disease, whether there is hyperlipidemia, whether there is renal insufficiency, whether there is ischemic stroke), lesion side, whether there is lower extremity arterial ulcers, lesion length, TASC classification, and degree of calcification. Preoperative hematological indicators included hemoglobin (Hb), white blood cell count (WBC), platelet count (PLT), fibrinogen (FIB), D-dimer (D-D), prothrombin time (PT), preoperative serum total cholesterol (TC), and preoperative triglyceride (TG) levels. Blood samples

were collected by drawing 4 mL of fasting venous blood from each patient before surgery, followed by centrifugation and serum separation. Hb, WBC, and PLT levels were measured using an automated blood cell analyzer. FIB, D-D, PT, activated partial thromboplastin time (APTT), and thrombin time (TT) were measured using an automated coagulation analyzer. TC and TG levels were measured using an automated biochemical analyzer.

Lesion types were determined based on preoperative CTA and patient history using the software Radiant. The severity of calcification was classified according to the peripheral vascular calcification scoring system from the patient's CTA as no calcification, mild calcification, or severe calcification. Lesion length was measured intraoperatively using the vascular quantitative analysis system integrated with the large digital subtraction angiography (DSA) machine.

Statistical methods

Sample size Estimation

The sample size was estimated using PASS 26.0, selecting the sample size comparison for a completely randomized design with two groups. When targeting an efficacy of 0.9 [12] and using a 1:2 ratio, the minimum sample size required was 76 patients in the recurrence group and 113 patients in the non-recurrence group, for a total of 189 cases in the training cohort. An additional 81 cases were selected for the validation cohort.

Statistical analysis

Statistical analyses were performed using SPSS 26.0 and R 3.6.2 software. Categorical data were expressed as n (%), and comparisons between the two groups were conducted using the chi-square test or Fisher's exact test. Continuous data were analyzed using the t-test or Mann-Whitney U test. Univariate analysis was performed using the log-rank χ^2 test, while multivariate analysis was carried out using logistic regression analysis. The selected variables were incorporated into a nomogram to construct a predictive model. The model was validated in both the training and validation cohorts using area under the curve (AUC) for prediction and calibration curves for verification. Decision curve analysis was conducted based on data from the training and validation cohorts to describe the net benefit of patients using the model. A P-value of < 0.05 was considered statistically significant.χ.

Results

Univariate analysis of the training group patients

A total of 270 patients with ASO who were treated at our hospital were retrospectively selected as study subjects. They were divided into a training cohort (189 cases) and a validation cohort (81 cases) based on a 7:3 ratio, shown in Fig. 1. In the training cohort of 189 patients, 76 (40.21%) were in the recurrence group and 113 (59.79%) in the non-recurrence group. In the validation cohort of 81 patients, 32 (39.51%) were in the recurrence group, and 49 (60.49%) were in the non-recurrence group. The results of the univariate analysis of the training group showed no significant differences between the recurrence and non-recurrence groups in terms of gender, smoking history, alcohol consumption history, coronary heart disease, hyperlipidemia, renal insufficiency, ischemic stroke, lesion side, lower extremity arterial ulcers, lesion length, TASC classification, calcification degree, intervention type, Hb, TC, PT, TT, and WBC (all $P > 0.05$). However, there were significant differences in age, BMI, diabetes, hypertension, lesion location classification, use of antiplatelet drugs, TG, FIB, and D-D ($P < 0.05$, respectively). See in Table 1.

Multivariate logistic regression analysis

The parameters with $P < 0.05$ from Table 1 were selected as independent variables and assigned values, such as age (≥ 60 years old = 1, < 60 years old = 0), BMI (≥ 24 kg/m² = 1, < 24 kg/m² = 0), diabetes (yes = 1, no = 0), hypertension (yes = 1, no = 0), lesion location classification (peripheral = 1, pelvic/femoral = 0), antiplatelet drug use (discontinued = 1, continued = 0), TG (actual value), FIB (actual value), and D-D (actual value). Whether ASO recurrence occurred after the intervention was set as the dependent variable (recurrence = 1, no recurrence = 0). The multivariate logistic regression analysis revealed that age ≥ 60 years, BMI ≥ 24 kg/m², diabetes, hypertension, discontinuation of antiplatelet drugs, FIB, and D-D were risk factors for the recurrence of ASO after intervention ($P < 0.05$). See in Table 2.

Risk prediction nomogram model

Based on the seven independent influencing factors identified, intergroup tests were conducted in both the training and validation cohorts. No statistically significant differences were found between the two groups for the significant variables (See in Table 3, $P > 0.05$). Using the results of the multivariate logistic regression analysis, a nomogram prediction model was constructed (Fig. 2). Each risk factor included in the nomogram was assigned a score, and the total score was generated by summing the values of each factor. The model was validated by inputting the training and validation cohort data into the established nomogram model. The model's AUC for the training cohort was 0.832, with a 95% confidence interval (CI) of 0.765–0.919 (Fig. 3A), while the AUC for the validation cohort was 0.858, with a 95% CI of 0.745–0.964 (Fig. 3B). The calibration curves showed a high degree of overlap between the predicted and actual curves in both cohorts, indicating good consistency between the model predictions and actual results (Fig. 4). The decision curve

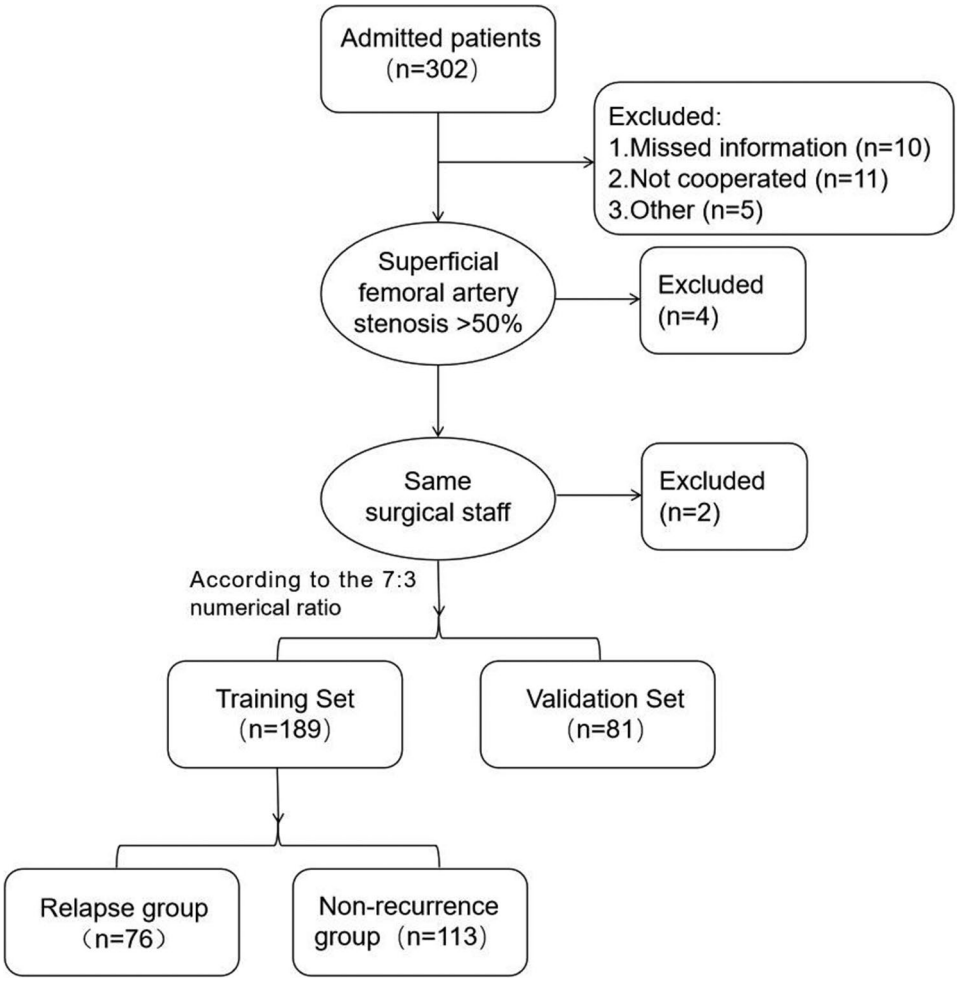

Fig. 1 Flowchart to select the study population

analysis demonstrated that the net benefit of the risk model in both groups was significantly higher than the "treat-all" and "no-treatment" curves, suggesting that the model has clinical applicability and can provide clinical benefits to patients (Fig. 5).

Discussion

Lower extremity ASO is a disease characterized by severe arteriosclerosis of the lower limb arteries, leading to lumen stenosis or even occlusion. The pathogenesis of the disease is related to endothelial cell damage and lipid deposition, and it is commonly seen in middle-aged and elderly individuals, often accompanied by risk factors such as smoking, diabetes, hypertension, and hyperlipidemia [13]. In severe cases, surgical intervention is required. Although minimally invasive surgery has the advantages of less trauma and faster recovery, there remains a certain risk of recurrence after the procedure [13, 14]. This study aimed to construct and validate a nomogram model for predicting the risk of recurrence in patients with lower extremity ASO after surgical intervention. In the univariate analysis, we found significant differences between the recurrence and non-recurrence groups in terms of age, BMI, diabetes, hypertension, lesion location classification, use of antiplatelet drugs, TG, FIB, and D-D ($P<0.05$, respectively). These variables may, to some extent, influence the risk of recurrence in ASO patients after surgical intervention.

Further multivariate logistic regression analysis revealed that age ≥ 60 years, BMI ≥ 24 kg/m^2, diabetes, hypertension, discontinuation of antiplatelet therapy, FIB, and D-D were independent risk factors for recurrence after surgical intervention in patients with lower extremity ASO ($P<0.05$, respectively). Age is an important risk factor, as the elasticity of the blood vessel walls gradually decreases with aging, and the endothelium becomes more susceptible to damage [15]. These physiological changes may accelerate the progression of arteriosclerosis, thereby increasing the risk of postoperative recurrence. Several studies have indicated that age is a significant factor influencing the recurrence of ASO after surgical intervention [15, 16]. Moreover, elderly patients

Table 1 Univariate analysis results of training group patients [n (%)]

Characteristics	Relapse group($n=76$)	Non-recurrence group($n=113$)	*P* value
Gender			> 0.05
Female	32 (42.11)	43(33.59%)	
Male	44 (57.89)	85(66.41%)	
Age (years)			< 0.05
< 60	24(31.58)	59(52.21)	
≥ 60	52(68.42)	54(47.79)	
BMI ≥ 24 kg/m^2	46 (60.53)	53(46.90)	< 0.05
Smoking history	53(69.74)	71(62.83)	> 0.05
Drinking history	51(67.11)	74(65.49)	> 0.05
Diabetes	54(71.05)	61(53.98)	< 0.05
Hypertension	56(73.68)	62(54.87)	< 0.05
Coronary heart disease	49(64.47)	70(61.95)	> 0.05
Hyperlipidemia	47(61.84)	71(62.83)	> 0.05
Renal insufficiency	45(59.21)	72(63.72)	
Ischemic stroke	44(57.89)	68(60.18)	
Classification of lesion location			< 0.05
Aortoiliac disease	21(27.63)	46(40.71)	
Femoropopliteal disease	12(15.79)	33(29.20)	
Surrounding type	43(56.58)	34(30.09)	
Pathological side (left side)	51(67.11)	73(64.60)	> 0.05
Lower limb arterial ulcer	33(43.42)	51(45.13)	> 0.05
Disease length/cm	7.93 ± 0.56	8.04 ± 0.67	> 0.05
TASC classification			> 0.05
A ~ B	20(26.32)	32(28.32)	
C ~ D	56(73.68)	81(71.68)	
Calcification degree			> 0.05
No calcification	21(27.63)	31(27.43)	
mild calcification	41(53.95)	60(53.10)	
Severe calcification	14(18.42)	22(19.47)	
Interventional procedure/			> 0.05
Simple balloon dilation	27(35.53)	40(35.40)	
Balloon dilation + stent implantation	49(64.47)	73(64.60)	
Antiplatelet drugs(used)	36(47.37)	82(72.57)	< 0.05
Hb /(g/L)	131.41 ± 17.12	129.42 ± 16.34	> 0.05
TC/(mmol/L)	4.81 ± 0.87	4.76 ± 0.80	> 0.05
TG/(mmol/L)	2.94 ± 0.56	1.70 ± 0.51	< 0.05
FIB/(g/L)	3.56 ± 0.55	3.02 ± 0.51	< 0.05
D-D/(mg/L)	0.76 ± 0.11	0.49 ± 0.09	< 0.05
PT/(s)	11.86 ± 2.12	12.06 ± 2.41	> 0.05
PLT/(×10^9/L)	255.13 ± 42.67	247.25 ± 40.87	> 0.05
TT/(s)	15.93 ± 4.22	16.21 ± 4.35	> 0.05
WBC/(×10^9/L)	7.71 ± 2.07	7.66 ± 2.11	> 0.05

BMI: Body Mass Index; TASC: Trans-Atlantic Inter-Society Consensus; Hb: Hemoglobin; TC: Total Cholesterol; TG: Triglyceride; FIB: Fibrinogen; D-D: D-dimer; PT: Prothrombin Time; PLT: Platelet; TT: Thrombin Time; WBC: White Blood Cell

are often accompanied by more chronic diseases such as hypertension and diabetes, which have also been identified as risk factors for recurrence following ASO surgery [17]. Obesity is a major risk factor for cardiovascular disease, and a high BMI may lead to elevated lipid levels, increasing the risk of atherosclerosis [18, 19]. Studies have shown that obesity can also impair endothelial cell function, promote inflammation, and contribute to thrombosis, thereby accelerating the recurrence of ASO after surgery [20, 21]. In diabetic patients, persistently elevated blood glucose levels may cause endothelial cell damage and exacerbate inflammatory responses. This damage may promote the formation and progression of atherosclerosis, thereby increasing the risk of recurrence following surgery [22–24]. Hypertension is one of the major risk factors for atherosclerosis. Persistent hypertension can lead to endothelial cell damage, exacerbate inflammatory responses, and cause vascular remodeling, which may promote the formation and progression of atherosclerosis, thereby increasing the risk of recurrence after ASO surgery [25]. In this study, both diabetes and hypertension were identified as risk factors, which is consistent with the findings of previous research [26]. The role of antiplatelet drugs in preventing thrombosis and reducing the progression of atherosclerosis has been widely recognized [27]. Our study also found that discontinuation of antiplatelet therapy was an independent risk factor for recurrence after surgical intervention in patients with ASO. Therefore, physicians should advise patients to continue taking antiplatelet medications to reduce the risk of thrombosis. FIB is a key component of the coagulation system, and elevated levels may promote thrombosis. In patients with ASO, elevated FIB levels may increase the risk of postoperative recurrence [28]. D-D, a product of fibrin degradation, may reflect a hypercoagulable state and an increased risk of thrombosis. In patients with ASO, elevated D-D levels may contribute to a higher risk of recurrence after surgery [29]. This study found that elevated FIB and D-D levels were associated with an increased risk of ASO recurrence after surgical intervention. Therefore, in clinical practice, it is important to regularly monitor patients' FIB and D-D levels to detect and manage potential coagulation abnormalities promptly.

Risk factors influencing the recurrence risk after surgical intervention in patients with ASO may promote the formation and progression of atherosclerosis through various mechanisms, thereby increasing the risk of postoperative recurrence. Therefore, active intervention and management of these risk factors in clinical practice are essential to reduce the recurrence risk for patients with ASO following surgical intervention. Although other approaches, such as machine learning models, have been used to predict postoperative risk in patients with lower extremity ASO, the nomogram model remains valuable in clinical practice due to its simplicity, intuitiveness, and ease of interpretation [30]. Based on the findings from this study, our team offers the following

Table 2 Multivariate logistic regression analysis

Variable	β value	SE value	Wald χ2 value	*P* value	OR value	95%CI
Age ≥ 60(years)	0.741	0.324	6.141	0.025	2.471	1.253, 3.465
BMI ≥ 24 kg/m^2	0.592	0.352	4.985	0.034	1.625	1.172, 3.098
Diabetes	1.572	0.397	14.391	0.002	4.568	2.175, 6.547
Hypertension	0.978	0.476	8.279	0.005	2.678	1.648, 4.287
Classification of lesion location	0.881	0.345	2.574	0.087	1.241	0.894, 2.114
Antiplatelet drugs	1.214	0.331	12.478	0.001	5.974	2.478, 8.246
TG/(mmol/L)	1.098	0.452	7.385	0.098	3.048	1.985, 4.655
FIB/(g/L)	0.987	0.374	6.297	0.002	2.073	1.347, 3.069
D-D/(mg/L)	1.087	0.498	9.844	0.011	3.067	1.257, 4.398

BMI: Body Mass Index; TG: Triglyceride; FIB: Fibrinogen; D: D-dimer; SE: Standard error; OR: Odds Ratio; CI: Confidence Interval

Table 3 Comparative analysis of modeling indicators for patients using the training set and validation set

Characteristics	Training Set(*n* = 189)	Validation Set(*n* = 81)	*P* value
Age (years)			> 0.05
< 60	83(43.92)	32(39.51)	
≥ 60	106(56.08)	47(58.02)	
BMI ≥ 24 kg/m^2	99(52.38)	41(50.62)	> 0.05
Diabetes	115(60.85)	49(60.49)	> 0.05
Hypertension	118(62.43)	48(59.26)	> 0.05
Classification of lesion location			> 0.05
Aortoiliac disease	67(35.45)	28(34.57)	
Femoropopliteal disease	45(23.81)	17(20.99)	
Surrounding type	77(40.74)	31(38.27)	
Antiplatelet drugs(used)	118(62.43)	47(58.02)	> 0.05
TG/(mmol/L)	2.16 ± 0.53	2.20 ± 0.56	> 0.05
FIB/(g/L)	3.32 ± 0.52	3.38 ± 0.53	> 0.05
D-D/(mg/L)	0.57 ± 0.09	0.58 ± 0.10	> 0.05

BMI: Body Mass Index; TG: Triglyceride; FIB: Fibrinogen; D: D-dimer

clinical insights: (1) Individualized Risk Assessment: The nomogram model provides clinicians and patients with an individualized tool for recurrence risk assessment. By inputting specific patient information, clinicians can quickly obtain a recurrence risk prediction for the patient post-intervention, thereby enabling more precise treatment and follow-up plans. (2) Risk Factor Management: This study identified several risk factors associated with recurrence after ASO intervention, including age, BMI, diabetes, hypertension, and discontinuation of antiplatelet medication. Clinicians should actively manage and intervene with these risk factors by controlling blood glucose and blood pressure, promoting lifestyle changes, and rationally using antiplatelet drugs to lower the recurrence risk. (3) Postoperative Follow-up and Monitoring: Enhanced follow-up and monitoring are essential for high-risk patients to detect and address possible recurrence promptly. Through regular check-ups and assessments, clinicians can monitor changes in the patient's condition, adjust treatment plans as needed, and ensure treatment efficacy. (4) Optimized Surgical Approach: Selecting an appropriate surgical approach is crucial for reducing recurrence risks. Clinicians should choose the most suitable surgical method, such as percutaneous interventional treatment or stent implantation, based on each patient's individual circumstance. (5) Patient Education and Self-Management: Patient education is an essential aspect of preventing ASO recurrence. Clinicians should educate patients on ASO-related information, including risk factors, treatment options, and lifestyle adjustments, to enhance patients' self-management capabilities [31].

Study Limitations: (1) The study adopted a single-center, retrospective design with training and validation sets, and a one-year follow-up period, which may introduce selection bias. Since the validation data is from our center, future multicenter studies with longer follow-up periods could help establish a more broadly applicable and accurate predictive model, possibly identifying additional meaningful predictors. (2) This study did not include a large number of laboratory parameters(e.g. C-reactive protein, Homocysteine) or predisposing risk factor(e.g. race, sedentary lifestyle, etc.)due to sample size limitations and the advanced age of the included patients, who often had multiple comorbidities. Including a large number of laboratory parameters might introduce bias, potentially affecting the model's predictive accuracy. Expanding the sample size and incorporating more laboratory parameters in future research would be beneficial.

In summary, this study successfully constructed a nomogram model for predicting the recurrence risk after surgical intervention in patients with lower extremity ASO, with predictions showing a good fit to actual outcomes. This model assists clinicians in better assessing and managing the risk of recurrence post-intervention in patients with ASO, achieving individualized patient predictions and providing valuable clinical utility for the precise treatment of lower extremity arteries.

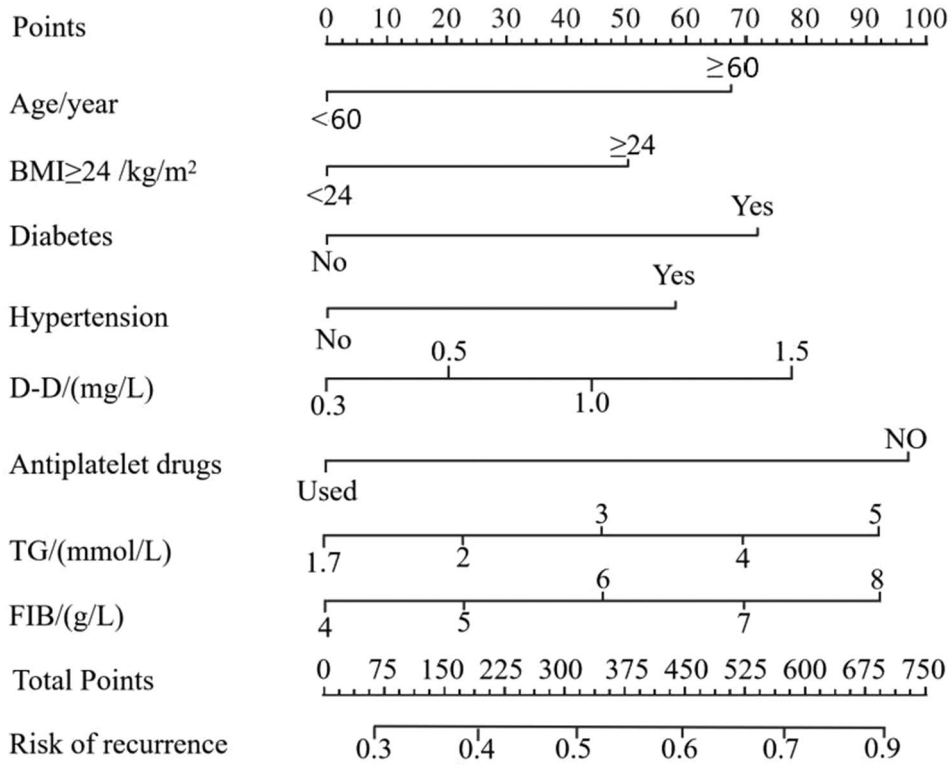

Fig. 2 Risk prediction column chart model BMI: Body Mass Index TG: Triglyceride FIB: Fibrinogen D: D-dimer

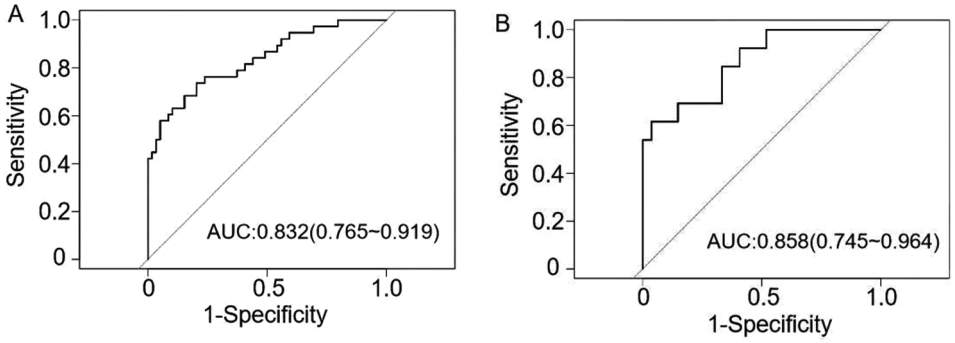

Fig. 3 Receiver operating characteristic curve and AUC of the column chart model. **A**: Receiver operating characteristic curve and AUC of the training set; **B**: Receiver operating characteristic curve and AUC of the validation set. AUC: Area Under Curve

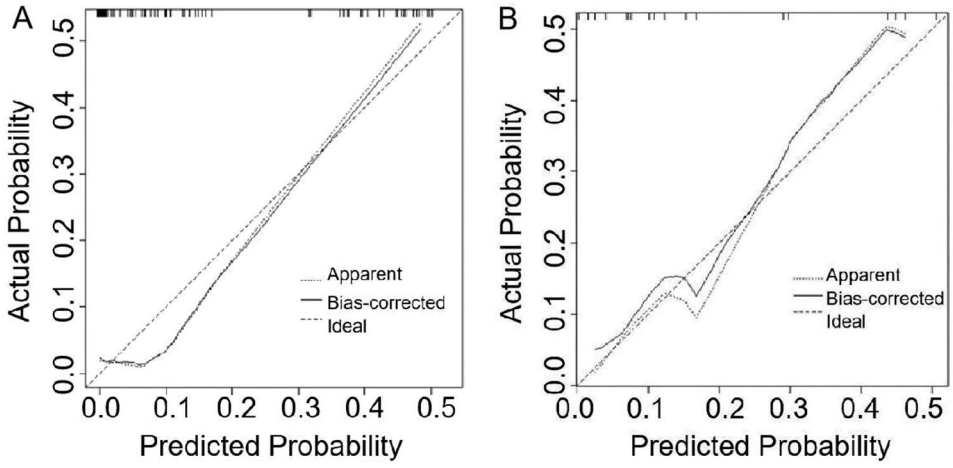

Fig. 4 Calibration curve for risk verification of column chart model. **A**: Calibration curve of the training set; **B**: Calibration curve of validation set

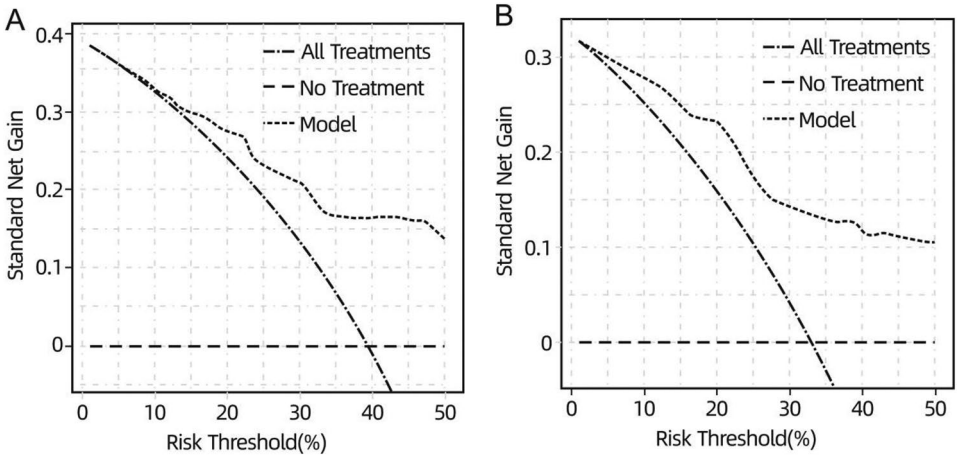

Fig. 5 Decision curves of the nomogram model in the training set and validation set. **A**: Decision Curve for the Training Set; **B**: Decision Curve for the Validation Set

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None.

Author contributions
Yanyan Lu wrote the manuscript. Lingyan Wang and Xiaoxiao Yu collected and analyzed the data. Xiaohu Meng revised the manuscript critically. All authors read and approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Competing interests
The authors declare no competing interests.

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