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Original Article

Predictive model construction for evaluating treatment outcomes of microscopic left internal spermatic vein reflux reconstruction plus left spermatic vein high ligation for grade III left varicocele and influencing factor prioritization

Peiyan Liu, Zhongxiang Liao, Zhonghong Liao, Jiangping Xie, Yanhua Wang, Feng Lin, Shulin Guo, Jinhua Wu

Department of Andrology, Ganzhou People's Hospital, Ganzhou 341000, Jiangxi, China

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Abstract: Objective: To investigate the factors influencing the efficacy of microscopic left internal spermatic vein reflux reconstruction (LISVRR) plus left spermatic vein high ligation (LSVHL) for grade III left varicocele. Methods: A total of 278 patients with degree III left-sided varicocele who underwent surgery at Ganzhou People's Hospital between January 2023 and December 2024 were retrospectively enrolled. Patients were randomly divided into a training cohort (70%, n = 195) and a validation cohort (30%, n = 83). General and clinical parameters were collected. Univariate analysis was first performed to identify potential predictors, followed by multivariate logistic regression to determine independent risk factors. Variable importance was ranked using the random forest algorithm. A nomogram prediction model was then developed, and its performance and clinical utility were evaluated using the concordance index (C-index) and decision curve analysis (DCA). Results: Multivariate analysis revealed that internal diameter of the spermatic vein, testosterone level and intraoperative blood loss were independent predictors of postoperative efficacy ($P<0.05$). The nomogram showed good discrimination in both the training (C-index = 0.794) and validation (C-index = 0.748) cohorts. DCA validated the model's clinical applicability. Conclusion: Internal diameter of the spermatic vein, testosterone level, blood flow velocity of the spermatic vein, and intraoperative blood loss are key factors affecting surgical efficacy of LISVRR plus LSVHL for grade III left varicocele. The developed prediction model demonstrates good predictive performance and potential clinical value.

Keywords: Varicocele, surgical efficacy, influencing factors, prediction models, random forest algorithm

Introduction

Varicocele, a common disease of the male genitourinary system, has a high prevalence, particularly degree III left-sided varicocele, posing substantial impact on male reproductive health [1]. Patients typically present with visibly dilated scrotal veins resembling a worm-like mass, accompanied by scrotal bulge, pain, and other discomfort, significantly impairing testicular spermatogenesis and leading to decreased sperm quality and increased infertility rates [2].

Microscopic left internal spermatic vein reflux reconstruction (LISVRR) combined with left spermatic vein high ligation (LSVHL) is currently an important surgical option for the treatment of grade III left-sided varicocele. The operation aims to improve blood reflux of the spermatic vein, reduce the adverse effect of varicosities on the testes, preserve testicular function, enhance semen quality, and partially restore fertility [3]. However, clinical outcomes vary considerably among patients, even with standardized surgical techniques [4]. While some experience marked symptom relief and significant improvement in semen quality postoperatively, others show limited or no benefit [5].

Currently, the factors influencing surgical efficacy remain insufficiently characterized, and no systematic research has prioritized their relative importance. Moreover, the lack of accurate and effective predictive models hampers pre-

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operative prognostic assessment, making it difficult to individualize treatment strategies and optimize therapeutic outcomes [6]. Therefore, identifying and ranking key determinants of surgical efficacy, and developing a validated prediction model for patients undergoing LISVRR plus LSVHL for grade III left-sided varicocele, hold significant clinical value for improving both surgical decision-making and prognosis [7].

Study population and methods

Participants

A total of 278 patients with degree III left-sided varicocele who underwent surgical treatment at Ganzhou People's Hospital between January 2023 and December 2024 were retrospectively enrolled. This study was approved by the Ethics Committee of Ganzhou People's Hospital.

Inclusion criteria: (1) Male; (2) Grade III left varicocele confirmed by physical examination and color Doppler ultrasound; (3) Age 18-50 years; (4) Complete clinical and follow-up data for analysis.

Exclusion criteria: (1) Absence of secondary sexual characteristics; (2) Concomitant bilateral varicoceles; (3) History of cryptorchidism or testicular tumor; (4) History of varicocele surgery (varicocelectomy); (5) Other diseases affecting semen quality (e.g., congenital testicular hypoplasia, duct obstruction); (6) Severe impairment of essential organ systems (e.g., cardiovascular, hepatic, and renal); (7) Recent treatments known to affect semen quality (e.g., radiotherapy, chemotherapy, hormone therapy).

Based on six-month follow-up data, patients were classified into either the favorable efficacy group or the unfavorable efficacy group. Favorable efficacy was defined as significant reduction or disappearance of scrotal bulge, significant improvement in semen quality (increased sperm concentration and motility, and reduced sperm deformity rate), and stable testicular volume. Unfavorable efficacy was defined as no significant improvement in or aggravation of scrotal bulge, no improvement or deterioration in semen quality, and a decreased testicular volume.

Methodology

Data acquisition: General information including age, height, weight, and body mass index (BMI), as well as disease course were collected. Color Doppler ultrasonography was used to measure the internal diameter of the spermatic vein and testicular volume, and to assess spermatic vein blood flow velocity and resistance index. Semen quality parameters, such as sperm concentration, sperm motility (percentage of progressively motile sperm), and sperm deformity rate, were collected. Serum hormone levels, including testosterone, follicle-stimulating hormone (FSH), and luteinizing hormone (LH), were measured. Patients were queried regarding comorbid chronic epididymitis, prostatitis, or other relevant conditions. Surgical indicators such as operative time and intraoperative blood loss were also documented.

Model building: Potential predictors of surgical efficacy were first screened using univariate analysis. Variables with $P<0.2$ were further subjected to multivariate logistic regression to identify independent predictors. The random forest algorithm was applied to rank the importance of these predictors. Based on logistic regression results, a nomogram predictive model was developed. A weighted point value was assigned to each predictor. The total score corresponded to an estimated probability of poor surgical efficacy, allowing individualized risk assessment.

Model evaluation and verification: The 278 patients were randomly allocated into a training set ($n = 195$) and a validation set ($n = 83$). In the training set, model discrimination was evaluated using the receiver operating characteristic (ROC) curve and area under the curve (AUC). Calibration was evaluated by comparing predicted and observed probabilities through calibration curves, and model fit was examined using the Hosmer-Lemeshow goodness-of-fit test. The C-index was calculated in the validation set to further assess discrimination. Clinical utility was evaluated using decision curve analysis (DCA), quantifying the net benefit of poor outcome predictions across a range of threshold probabilities.

Statistical methods

Data analyses were conducted with SPSS 26.0 and R 4.2.1 software packages. Measurement

Table 1. Comparison of patient characteristics between the training and validation sets

Index	Training set (n = 195)	Validation set (n = 83)	statistical values	*P* value
Age (years)	28.23±5.14	29.24±5.68	1.452	0.147
BMI (kg/m^2)	23.68±3.32	24.35±3.56	1.506	0.133
Course of disease (years)	4.21±1.35	4.52±1.83	1.567	0.118
Internal diameter of spermatic vein (mm)	5.12±0.65	5.27±0.94	1.530	0.127
Sperm concentration (× 10/mL)	42.25±10.53	40.24±8.51	1.537	0.125
Sperm motility (%)	48.03±11.25	45.78±9.01	1.602	0.110
Sperm deformity rate (%)	40.78±6.24	42.53±8.56	1.904	0.057
Testicular volume (mL)	18.5±3.21	17.78±2.83	1.844	0.066
spermatic vein blood flow velocity (cm/s)	26.52±5.54	25.67±4.58	1.230	0.219
Resistance index	0.67±0.12	0.73±0.45	1.726	0.085
Testosterone (nmol/L)	16.03±3.52	15.57±2.84	1.053	0.293
Follicle stimulating hormone (IU/L)	5.27±1.26	5.58±1.54	1.753	0.081
Luteinizing hormone (IU/L)	4.27±1.11	4.56±1.35	1.865	0.063
Combined chronic epididymitis (Yes/No, case)	39/156	18/65	0.138	0.710
Combined prostatitis (yes/no, case)	38/157	21/62	1.177	0.277
Operation time (min)	75.23±12.21	78.54±15.67	1.894	0.059
Intraoperative blood loss (mL)	33.78±6.21	35.54±8.56	1.920	0.055

data with a normal distribution were reported as mean ± standard deviation ($\bar{x}$ ± s) and compared using independent samples t-test. Non-normally distributed continuous variables were presented as median (Q1, Q3) and analyzed with the Mann-Whitney U test. Enumeration data were expressed as counts (n) and percentages (%), with comparisons conducted using the χ^2 test or Fisher's exact test, as appropriate.

Multivariate logistic regression analysis was performed to identify independent predictors of surgical efficacy. The random forest algorithm was implemented using the "randomForest" package in R to rank predictor importance. The "rms" package was applied for nomogram construction, "pROC" package for ROC curve plotting, "ggplot2" package for calibration curve generation, and "DCA" package for decision curve analysis.

Results

Inter-group comparison of general data

There were no significant differences between the training set and validation set in baseline characteristics, including age, BMI, and most laboratory indicators (P>0.05; **Table 1**).

Univariate analysis of factors associated with surgical efficacy

Univariate analysis showed that the course of disease, internal diameter of the spermatic vein, sperm concentration, sperm viability, sperm deformity rate, testicular volume, spermatic vein blood flow velocity, testosterone level, chronic epididymitis, and intraoperative blood loss were associated with surgical efficacy (P<0.05; **Table 2**).

Multivariate logistic regression analysis of surgical outcome determinants

Multivariate Logistic regression analysis was performed with unfavorable surgical efficacy as the dependent variable (0 = absent, 1 = present) and the significant variables (P<0.05) from the univariate analysis as covariates. The results showed that disease course, internal diameter of the spermatic vein, sperm concentration, spermatic vein blood flow velocity, testosterone level, and intraoperative blood loss were independent predictors of surgical outcome (P<0.05). In regression modeling, all predictor variables exhibited tolerance values exceeding 0.1, variance inflation factors (VIF) <10, and condition indices <30. In addition, over half of the covariates demonstrated variance proportions without shared characteristic

Table 2. Univariate analysis of surgical efficacy

Index	Favorable efficacy group (n = 144)	Unfavorable efficacy group (n = 51)	Statistical values	*P* value
Age (years)	27.34±5.34	28.52±5.83	1.323	0.187
BMI (kg/m^2)	23.41±3.26	24.13±3.25	1.356	0.176
Course of disease (years)	3.75±1.43	4.52±1.83	3.061	0.002
Internal diameter of spermatic vein (mm)	4.98±0.63	5.27±0.92	2.483	0.013
Sperm concentration (× 10/mL)	42.25±10.62	37.54±8.52	2.856	0.004
Sperm motility (%)	48.53±11.05	43.23±9.12	3.073	0.002
Sperm deformity rate (%)	39.21±6.35	42.13±8.56	2.563	0.011
Testicular volume (mL)	18.56±3.27	17.63±2.86	1.801	0.073
Spermatic vein blood flow velocity (cm/s)	26.03±5.54	23.58±4.57	2.833	0.005
Resistance index	0.66±0.17	0.73±0.33	1.928	0.055
Testosterone (nmol/L)	16.21±3.57	14.53±2.86	3.032	0.002
Follicle stimulating hormone (IU/L)	5.24±1.26	5.57±1.35	1.577	0.116
Luteinizing hormone (IU/L)	4.26±1.13	4.55±1.36	1.491	0.137
Combined chronic epididymitis (Yes/No, case)	22/122	17/34	7.673	0.005
Combined prostatitis (yes/no, case)	25/119	13/38	1.586	0.207
Operation time (min)	75.23±1213	78.56±15.35	1.567	0.118
Intraoperative blood loss (mL)	32.03±6.24	35.18±8.21	2.841	0.005

Table 3. Multivariate analysis of surgical efficacy

Factor	*B*	Standard error	*Wald*	*P*	*OR*	95% confidence interval
Course of disease	0.372	0.124	8.980	0.003	1.451	1.137-1.851
Internal diameter of spermatic vein	0.524	0.247	4.498	0.034	1.689	1.041-2.742
Sperm concentration	-0.056	0.020	7.734	0.005	0.945	0.908-0.983
Spermatic vein blood flow velocity	-0.075	0.035	4.570	0.033	0.927	0.865-0.994
Testosterone	-0.162	0.057	7.934	0.005	0.851	0.760-0.952
Intraoperative blood loss	0.059	0.027	4.877	0.027	1.061	1.007-1.118
Constant	-0.686	2.223	0.095	0.758	0.504	

Table 4. Variable assignment table

Variable		Assignment
X1	Course of disease	continuous variable
X2	Internal diameter of spermatic vein	continuous variable
X3	Sperm concentration	continuous variable
X4	Spermatic vein blood flow velocity	continuous variable
X5	Testosterone	continuous variable
X6	Intraoperative blood loss	continuous variable
Y	Unfavorable surgical efficacy	No = 0, yes = 1

values, indicating that multicollinearity was not a concern in this model (**Table 3**).

Prioritization of factors influencing surgical efficacy based on a random forest algorithm

A random forest model was constructed incorporating the independent factors identified in multivariate analysis (the variable assignment is shown in **Table 4**). The ranking of variable importance was as follows: testosterone > disease course > internal diameter of spermatic vein > intraoperative blood loss > sperm concentration > spermatic vein blood flow velocity.

Stepwise random forest analysis revealed that the optimal out-of-bag (OOB) error rate was achieved when these six variables were included (**Figure 1**). There are three curves in the figure, which correspond to OOB and the labels of the outcome events in our dataset. As can be seen from the figure, as the number of trees increases, the OOB value gradually decreases

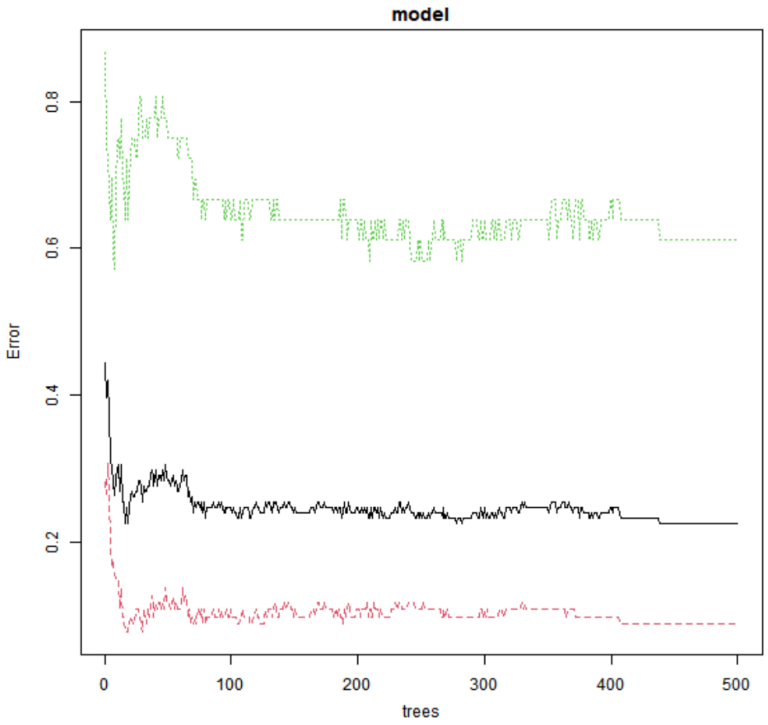

Figure 1. Relationship between model error rate and number of decision trees. Red: favorable surgical efficacy; Black: Out-of-Bag (OOB) error rate; Green: unfavorable surgical efficacy.

and stabilizes. Similarly, it can be observed that the classification error rate for the outcome events (1: unfavorable surgical efficacy, 0: favorable surgical efficacy) also stabilizes after this tree range. Consequently, they were included in predictive modeling using both the random forest algorithm and multivariate Logistic regression. The mean reduction in Gini index for each variable corresponded directly to its relative importance in the model (**Figure 2A**).

Surgical efficacy prediction model establishment

Based on independent predictors identified through multivariate analysis, a nomogram prediction model was developed. Each risk factor was assigned a weighted score, with the cumulative total score corresponding to the prognostic probability of unfavorable surgical outcomes. Higher total scores indicated a greater likelihood of unfavorable efficacy (**Figure 2B**).

Model assessment and validation

The C-index values of the nomogram model achieved 0.794 in the training cohort and 0.748 in the validation cohort. Calibration plots demonstrated close agreement between predicted and observed outcomes. Hosmer-Lemeshow goodness-of-fit testing showed χ^2 = 5.265 (P = 0.728) in the training set and χ^2 = 11.608 (P = 0.169) in the validation set. ROC curve analysis yielded an AUC of 0.794 (95% CI: 0.723-0.885, 75% sensitivity, 73.3% specificity) in the training set and 0.749 (95% CI: 0.601-0.897; 66.7% sensitivity, 69.8% specificity) in the validation set. Calibration and ROC curves are presented in **Figures 3**, **4**, respectively.

Decision curve analysis of the nomogram prediction model

Decision curve assessment (**Figure 5**) demonstrated that the nomogram model offered greater net clinical benefit compared with the "treat all" or "treat none" strategies in predicting surgical efficacy for grade III left varicocele. The model's advantage maintained consistency for threshold probabilities spanning from 0.08 to 0.95.

Discussion

Varicocele is a common disorder of the male genitourinary system, occurring more frequently in infertile men. Grade III left-sided varicocele significantly impairs testicular function, manifesting as scrotal bulging, pain, and decreased sperm quality, ultimately compromising male fertility [8]. Microscopic LISVRR plus LSVHL is an important method aimed at improving spermatic vein reflux and preserving testicular function [9]. However, postoperative efficacy varies substantially among patients. While some recover well after surgery, with obvious symptom relief and improved semen quality, others continue to present with persistent symptoms and limited functional recovery [10]. Thus, this study seeks to identify prognostic determinants, rank their importance, and develop predictive models to guide individualized treatment strategies and improve outcomes.

Multivariate Logistic regression analysis identified spermatic vein internal diameter, testoster-

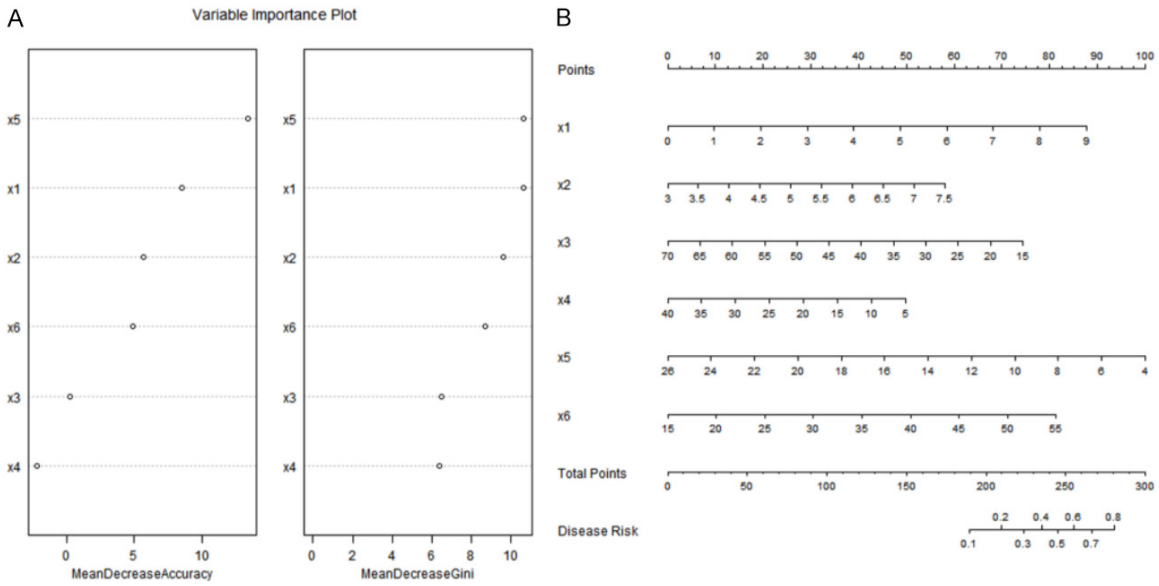

Figure 2. Ranking of importance of influencing factors and the nomogram prediction model for surgical efficacy in Grade III left-sided varicocele. A: Ranking of importance of influencing factors; B: The nomogram prediction model. Notes: x1: course of disease; X2: inner diameter of spermatic vein; X3: sperm concentration; X4: spermatic vein blood flow velocity; X5: testosterone; X6: intraoperative bleeding volume.

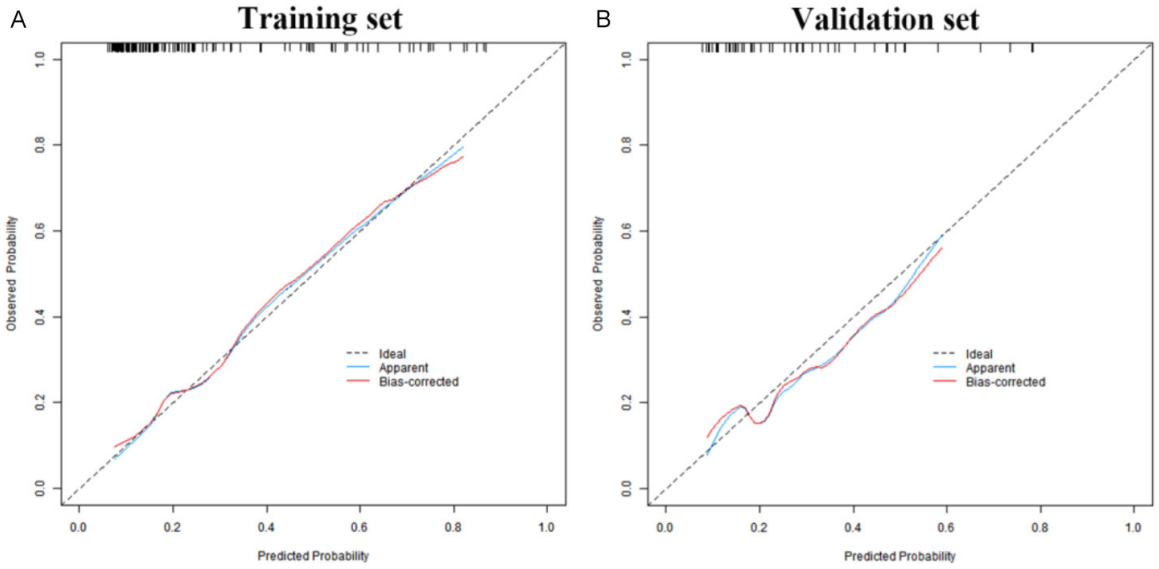

Figure 3. Calibration curve for the predictive model in both training (A) and validation (B) set.

one level, and intraoperative blood loss as independent predictors of surgical efficacy. Among them, testosterone level ranked first in importance according to the random forest algorithm, underscoring its clinical significance. As an important reproductive hormone in men, it is critical in maintaining normal testicular spermatogenic function and reproductive metabolism [11]. In patients with grade III left-sided varicocele, the testicular microenvironment is altered due to impaired spermatic vein blood perfusion, potentially compromising testosterone synthesis and secretion, which in turn diminishes spermatogenic function [12]. Although surgery can improve venous return, the low testosterone level before surgery may indicate advanced testicular damage, limiting postoperative functional recovery. Previous studies

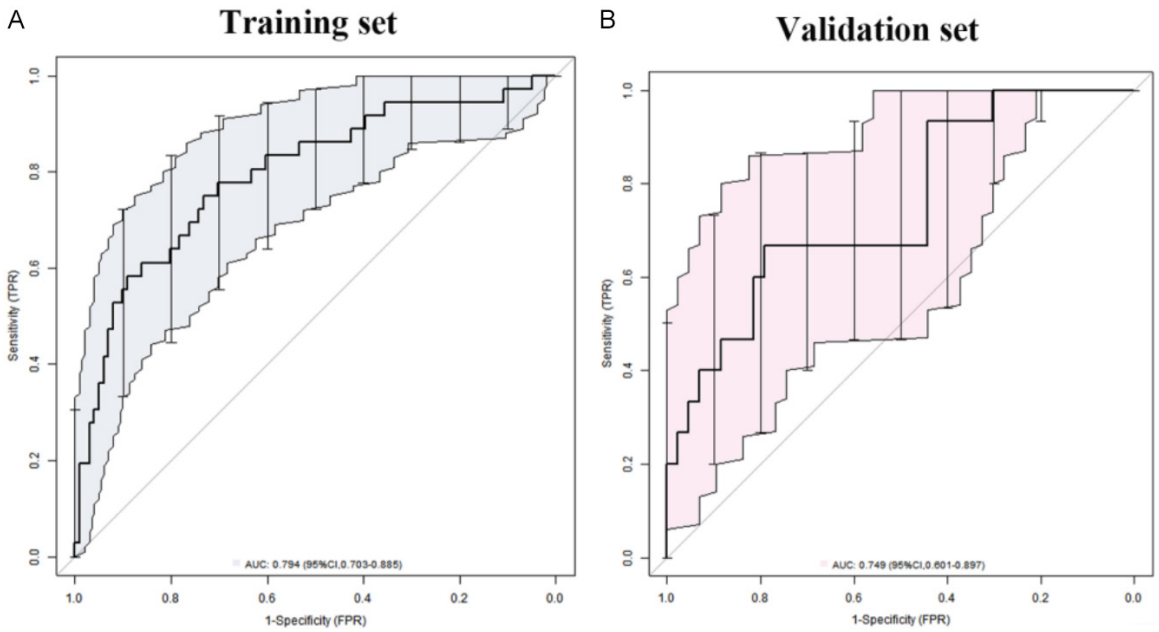

Figure 4. ROC curves for the nomogram in predicting surgical outcome in both training (A) and validation (B) sets.

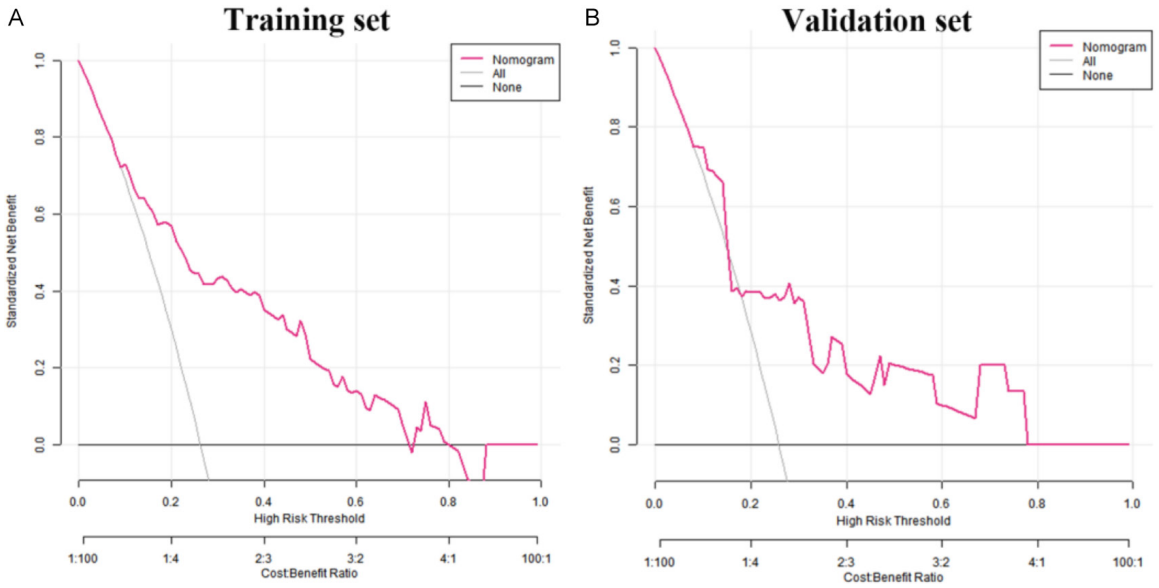

Figure 5. Decision curve analysis for the nomogram in both training (A) and validation (B) sets.

have linked reduced testosterone levels with decreased sperm density and motility, and our findings similarly showed that surgical intervention failed to markedly enhance semen quality in patients with low testosterone concentrations, further confirming its important role in determining surgical efficacy [13].

The internal diameter of the spermatic vein is another key determinant affecting surgery efficacy. A larger diameter generally indicates a more severe varicocele, which exerts greater compression on the testes and disrupts venous return. Long-term poor blood return can cause hypoxia in testicular tissue and accumulation of metabolic wastes, damaging the spermatogenic and Sertoli cells, thereby impairing sperm generation and maturation [14]. Although surgical ligation can correct the reflux, the extent of functional recovery in already damaged testicu-

lar tissue may be limited. A larger preoperative internal diameter of spermatic vein is therefore associated with more extensive testicular injury and more difficult postoperative testicular function recovery, ultimately reducing the likelihood of a favorable outcome. This observation aligns with prior research, suggesting that clinicians should attach great importance to the index of the internal diameter of the spermatic vein in preoperative evaluation [15].

Intraoperative blood loss is also an important factor affecting surgical efficacy. Excessive intraoperative bleeding may induce local tissue hypoxia and ischemia, impairing testicular blood supply and nutrient delivery, thereby delaying postoperative testicular function recovery [16]. Massive bleeding may also trigger local inflammatory reactions and tissue adhesions, which may further compromise blood return to the spermatic vein and testicular physiology. In addition, excessive bleeding may increase surgical risk, prolongs operation time, and negatively affect the overall condition of the patient. Therefore, meticulous surgical technique, minimization of intraoperative bleeding, and protection of surrounding tissues and blood vessels are essential to optimizing postoperative outcomes.

DCA further demonstrated the model's significant clinical utility within a defined range of threshold probabilities. This suggests that clinicians can utilize the model's prognostic estimates and patient-specific factors to formulate tailored perioperative management strategies. For high-risk patients, proactive preoperative measures, such as lifestyle modification, nutritional supplementation, and management of comorbidities, may enhance procedural success [17]. In addition, postoperative surveillance can facilitate timely detection and management of complications.

There are some limitations to this study. First, external verification was not performed, which may be related to the limited sample size. The relatively small cohort may not cover all possible factors influencing surgical efficacy, thereby restricting the predictive ability of the model. Second, variables analyzed in this study may not be comprehensive enough. Some potential determinants, such as genetic polymorphisms, lifestyle factors (e.g., smoking, alcohol consumption, long-term sitting), and environmental factors, were not taken into account [18]. Third, follow-up was limited to the short term. Given that recovery of testicular function after varicocele surgery may take a long time, and there is a certain risk of recurrence, the absence of long-term outcome data limits the ability to fully assess both surgical efficacy and the predictive ability of the model. Future research should expand sample size, include additional potential contributing factors, and conduct multi-center research with extended follow-up to refine the model, enhance prediction accuracy, and minimize error.

Conclusion

Internal diameter of the spermatic vein, testosterone level and intraoperative blood loss are independent predictors of surgical efficacy in patients undergoing microscopic LISVRR combined with LSVHL for grade III left-sided varicocele. The established predictive nomogram model demonstrated favorable predictive performance and clinical application value. Nonetheless, further improvement and optimization is warranted. Future studies should focus on increasing the sample size, incorporating more influencing factors, and conducting multi-center studies and long-term follow-up to improve the model's accuracy, reliability, and clinical applicability.

Disclosure of conflict of interest

None.

Address correspondence to: Jinhua Wu, Department of Andrology, Ganzhou People's Hospital, Ganzhou 341000, Jiangxi, China. Tel: +86-0797-6120120; E-mail: 13697010617@163.com

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