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Construction and Evaluation of a Predictive Nomogram for Identifying Premature Failure of Arteriovenous Fistulas in Elderly Diabetic Patients

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Background: This research aimed to identify risk factors contributing to premature maturation of arteriovenous fistulas (AVF) in elderly diabetic patients and develop a clinical prediction model.

Methods: We conducted a retrospective review of 548 geriatric diabetic patients who underwent AVF creation for maintenance hemodialysis (MHD) at Baoding No 1 Central Hospital between January 2011 and December 2023. Patients were divided into mature (386) and immature (162) groups based on AVF maturation status. Univariate logistic regression analysis and the least absolute shrinkage and selection operator were used to identify independent risk factors, including D-dimer levels, low-density lipoprotein cholesterol levels, internal radial meridian, radial artery plaque presence, and cephalic vein indwelling needle use history. A predictive nomogram was developed specifically for immature AVF in elderly diabetic patients. Model performance was evaluated using the area under the receiver operating characteristic curve (AUROC), calibration curve, decision curve analysis (DCA), and clinical impact curve (CIC).

Results: Among elderly patients with diabetes mellitus, the incidence of immature AVF was 29.56%, affecting 162 of 548 individuals. The five-variable model demonstrated an AUROC value of 0.922, with a 95% confidence interval (CI) of 0.870 to 0.947 in the training dataset, and an AUROC of 0.912, accompanied by a 95% CI of 0.880 to 0.935 in the internal validation dataset. The calibration curve, derived from 1000 bootstrap samples, showed good agreement between predicted and observed outcomes. Additionally, both the DCA and CIC exhibited favorable clinical utility and net benefits.

Conclusions: The nomogram prediction model, based on independent risk factors, serves as a valuable tool for accurate prognosis and has potential to aid in establishing and preserving hemodialysis access in elderly diabetic patients, ultimately optimizing their healthcare outcomes.

Keywords: arteriovenous fistula, vascular access, hemodialysis, diabetes, nomogram

Introduction

For patients undergoing maintenance hemodialysis (MHD), the arteriovenous fistula (AVF) remains the preferred vascular access modality. According to the Dialysis Outcomes and Practice Patterns Study, AVF comprises a significant 88.2% of all vascular access methods employed in China.[1] However, immediate utilization of AVF post-creation is often precluded by the necessary maturation period. Typically, an AVF undergoes a maturation phase spanning approximately 4 to 8 weeks following surgery. A comprehensive meta-analysis, reviewing over 8000 studies and focusing on 318 in particular, yielded concerning findings. It was ascertained that only 26% of fistulas achieved maturity at the 6-month mark, while a concerning 21% were ultimately decommissioned due to non-utilization.[2] Johannes W and his team conducted a prospective cohort study to investigate the outcomes of establishing vascular access in octogenarian

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patients. Their research revealed that the octogenarian cohort experienced the highest primary failure rate of AVF, with a notable proportion of 42.1%.[3] These failures often necessitate the insertion of a central venous catheter for MHD, a procedure that may precipitate complications such as superior vena cava stenosis and catheter-related infections, ultimately augmenting the risk of all-cause mortality.[4]

Over the past three decades, notable shifts in patient demographics have been documented. Specifically, a substantial proportion of the geriatric population, defined as individuals aged 65 and above, has been identified to suffer from diabetes mellitus or prediabetes. Precisely, more than 25% of this demographic cohort have diabetes, and approximately 50% have prediabetes. In 2019, China harbored approximately 33.5 million geriatric patients with diabetes aged 65 and older, ranking first globally and accounting for one-fourth of the worldwide total.[5,6] Diabetes mellitus has emerged as a pressing health concern, representing the fastest-growing contributor to the incidence of chronic kidney disease (CKD) worldwide.[7] Among diabetics, the incidence of diabetic kidney disease (DKD) ranges between 20% and 50%. Clinically, DKD is characterized by persistent albuminuria and/or a progressive decline in glomerular filtration rate, ultimately progressing to end-stage renal disease (ESRD). DKD is recognized as the primary cause of ESRD and renal replacement therapy (RRT). For instance, in the United Kingdom, DKD-related ESRD accounts for 28% of RRT patients, whereas in the United States and Australia, the figures are 44% and 38%, respectively.[8] In mainland China, the number of DKD-ESRD patients stood at approximately 1.06 million in 2015, significantly surpassing ESRD cases attributed to other etiologies.[9] However, it is crucial to acknowledge that DKD-ESRD represents only a subset of patients with diabetes who have progressed to CKD stage 5. There are numerous other causes of ESRD in patients with diabetes, including chronic glomerulonephritis, lupus nephritis, and other conditions.

Investigating a predictive model for immature AVF in elderly diabetic patients undergoing MHD is crucial. Despite numerous studies examining risk factors for AVF complications in this patient cohort, a clear consensus has yet to be established. Specifically, factors such as aging and diabetes can negatively impact AVF maturation by influencing underlying vascular conditions.[10–15] Furthermore, peripheral ischemic disease exhibits a heightened predisposition to manifest in diabetic patients undergoing dialysis. Claudia Altobelli et al[16] through a multicenter investigation, elucidated that Rheopheresis effectively mitigated overall pain levels. Their data also hinted at its potential to either rehabilitate or ameliorate ulcers and hemorheological laboratory parameters among MHD patients suffering from peripheral artery disease and ischemic ulcers that have proven refractory to standard therapeutic interventions. The presented column graph effectively visualizes the analysis results derived from a Logistic regression model, translating risk factors into scores. This approach enables a personalized and accurate prediction of potential adverse events, offering a highly intuitive and visually appealing prediction tool.[17] Previous studies have demonstrated the efficacy of prediction models in various medical contexts,[18–21] particularly in MHD patients, where models predicting complications and mortality have been extensively explored.[22–25] However, the prediction of immature AVF remains relatively scant. Yufeng Liang et al[26] conducted a comprehensive cohort study encompassing 238 individuals diagnosed with CKD stage 5. Their objective was to develop a novel nomogram prediction model specifically tailored for forecasting the likelihood of inadequate AVF maturation in this patient cohort. Their model incorporates five key indicators: ICVM, radial artery velocity, TC level, hypertension, and diabetes. This model achieved an AUC of 0.848, indicating its strong predictive performance. However, the study's scope was limited, primarily focusing on demographic characteristics, and further exploration of additional factors is warranted. In another research endeavor, Kumar J.S. and his team[27] aimed to create a predictive model for identifying premature or non-mature AVF in patients with diabetic nephropathy. Their model considered factors such as palpable wall tremor of the radial artery, small radial artery diameter, peak velocity of radial artery contraction (PSV<45cm/s) and linear calcification of the radial artery. However, the model's simplicity in combining indicators (assigning positive values as 1 and negative values as 0) and incorporating the total score into a binary logistic regression may have compromised its predictive efficiency. Additionally, the small sample size of only 31 cases with immature AVF limits the model's generalizability. In conclusion, while progress has been made in predicting AVF maturation, there is still a need for more comprehensive and accurate models that consider a wider range of factors and employ more sophisticated analytical techniques.

Therefore, the elderly patients with diabetes and CKD5 are poorly represented in clinical trials,[6] making individualized prediction a challenging clinical problem. Exploring risk models pertaining to immature AVF in this patient

population holds paramount clinical importance. To our understanding, this investigation represents the pioneering study to explore the risk factors contributing to premature AVF maturation in elderly patients with diabetes and CKD stage 5, as well as the construction of a nomogram prediction model. Our methodology employed routine clinical features and standard blood test results to formulate a probabilistic model designed to forecast AVF maturation. The overarching objective is to provide evidence-based support for the establishment and preservation of vascular access in this distinct patient cohort. Below, we present the detailed outcomes of our research.

Clinical Subjects and Study Design

General Information

We collected clinical data on 1620 geriatric patients with diabetes mellitus who underwent AVF surgery during their nephrology ward admissions at Baoding First Central Hospital, spanning from January 1, 2011, to December 31, 2023. The aim was to investigate the incidence rate of AVF maturation failure. This research project was approved by the institutional Ethics Committee of Baoding First Central Hospital, under approval number Kuai [2023]066.

Inclusion Criteria

(1) Age ≥60 years, diagnosed diabetes, gender is not limited; (2) The lateral limb of the intended AVF is the first AVF; (3) The proposed operation was an end-to-side carpal cephalic vena-radial anastomosis of AVF. Exclusion criteria: (1) The central venous catheter was placed in the limb of the proposed AVF for > 2 months; (2) Combined with peripheral vascular disease, severe cardiopulmonary diseases or pre-survival ≤4 months; (3) Occlusion during AVF observation.

Surgical Procedures for AVF

Prior to surgery, we conducted Allen's test and ultrasound examinations on each patient to assess the vascular status of the upper limb intended for AVF creation. For the creation of a AVF, if the diameters of the radial artery and cephalic vein are more than 1.5 mm, or if the Allen's test result is normal, it is generally considered suitable to perform AVF surgery. All surgeries were performed by an experienced surgeon, holding qualifications of associate chief physician or above, with over three years of surgical practice. The left radio-cephalic AVF of the upper extremity was chosen for the procedure. The patient's left upper limb was rotated outwards, followed by thorough disinfection and preparation. Local infiltration anesthesia was administration using 2% lidocaine. A longitudinal incision of approximately 4 cm was made at the proximal end of the left wrist. The subcutaneous tissue was dissected meticulously, layer by layer. The cephalic vein measured approximately 4 cm, while the radial artery spanned about 2cm. The radial artery was temporarily clamped using ophthalmic bending forceps. The distal cephalic vein was ligated, and the proximal segment was excised. Using a scalpel, an approximately 8mm section of the lateral wall of the radial artery was dissected. A distal vein-radial anastomosis was performed, and the ophthalmic bending forceps were subsequently removed. The skin was sutured after a local tremor ensured the patency of the AVF.

AVF Mature Evaluation Methods and Criteria

Evaluation Technique

The assessment of AVF maturity was conducted between six and twelve weeks postoperatively. This examination utilized the Philips EPIQ 7C color Doppler ultrasound system, employing a linear array transducer operating at a frequency of 10 MHz. The patient was positioned in the supine position with relaxed muscles and the examination area fully exposed. The handheld transducer was placed perpendicular to the skin over the AVF for inspection. The initial step involved a two-dimensional measurement of the anastomotic diameter. Subsequently, the flow patterns of the inflow and outflow vessels, their luminal dimensions, and any intraluminal or extraluminal echoes were meticulously examined to detect potential signs of thrombosis, vascular calcification, or stenosis. Additionally, pulse-wave Doppler ultrasonography was employed to assess the blood flow spectrum and velocity index, enabling the system to automatically calculate the intravascular blood flow characteristics.

The Criteria for Assessing AVF Maturity in China are as Follows

If the ultrasound or clinical indicators of maturity are not met within 6–12 weeks following AVF surgery, the AVF is considered to have inadequate maturity. For ultrasound criteria, an AVF is deemed mature if it has a natural blood flow rate exceeding 500mL/min, an internal diameter of the puncture section measuring at least 5mm, and a depth from the skin surface of less than 6mm, six weeks post-operation. For clinical criteria, sufficient blood flow, maintained at a rate of at least 250mL/min throughout the dialysis process, is required twelve weeks after surgery. The blood flow rate must support a minimum of three hemodialysis sessions weekly. A blood flow rate is considered insufficient if, during hemodialysis, the pump-controlled flow rate drops below 200 milliliters per minute. Our research, based on Chinese standards, indicates that failure to meet either clinical or ultrasonic criteria for maturity is indicative of AVF immaturity.

Comprehensive Compilation of Observation Indicators

Acquire a wide range of clinical data from electronic health records, outpatient records, and telephonic follow-ups, including:

Demographic Factors

Information on Age, Gender, Body Mass Index (BMI), Smoking Status, Medical History of cardiovascular and cerebrovascular diseases (CVD), hypertension, and the presence of cephalic vein indwelling needle use history (CVIN).

Biochemical Parameters

Analysis of Red Blood Cell (RBC) counts, White Blood Cell (WBC) counts, Platelet (PLT) counts, Neutrophil (NEU) and Lymphocyte (LYM) counts; Measurement of Erythrocyte Distribution Width (RDW); Levels of Hemoglobin (HB), Plasma D-Dimer (D-D), Fibrinogen Degradation Products (FDP), Albumin (ALB), Serum Creatinine (SCR), Blood Urea Nitrogen (BUN), Blood Uric Acid (BUA), Pro-brain Natriuretic Peptide (Pro-BNP); Assessment of Triglycerides (TG), Low-Density Lipoprotein (LDL), Total Cholesterol (TC), Fasting Plasma Glucose (FBG), Parathyroid Hormone (PTH), Procalcitonin (PCT), C-reactive Protein (CRP); Evaluation of Erythrocyte Sedimentation Rates (ESR); Calculation of Neutrophil to Lymphocyte Ratios (NLR), Platelet to Lymphocyte Ratios (PLR), Platelet to Albumin Ratios (PAR); Consideration of Indices such as Prognostic Nutritional Index (PNI) and Triglyceride Glucose Index (TYG).

Imaging Metrics

Assessment of Left Ventricular Ejection Fraction (LVEF), Internal Radial Meridian (IRM) measurements, Internal Cephalic Vein Meridian (ICVM) measurements, and evaluations of Radial Artery Plaque (RAP).

Statistical Methodology

Data manipulation was facilitated using SPSS (version 26.0) and R software (version 4.1.3). All statistical inferences were conducted on a bilateral basis, adopting a significance threshold of $p < 0.05$.

To Evaluate the Normality of the Data Distribution, the Shapiro–Wilk Test Was Utilized

Data was considered normally distributed if the resulting p-value was ≥ 0.05. For normally distributed data, descriptive statistics were reported as the mean ± standard deviation ($x \pm s$), and comparisons between two independent samples were conducted using the Student's *t*-test. Conversely, data that did not adhere to a normal distribution were represented by the median, along with the 25th and 75th percentiles [M (P25, P75)], and analyzed using the Mann–Whitney *U*-test. Categorical data were summarized using frequencies or ratios, with the χ^2-test applied for statistical analysis. To identify potential predictor variables, a univariate logistic regression model was employed, and only variables with statistical significance ($p < 0.05$) were considered for inclusion in the least absolute shrinkage and selection operator (LASSO) model. Potential independent predictors of impaired AVF maturation in elderly diabetics were screened, and odds ratios (ORs) with their corresponding 95% confidence intervals (CIs) were calculated.

Utilizing R Software, a Prediction Model Was Constructed Incorporating Variables Identified as Non-Zero Coefficients in the LASSO Process

Internal validation of this model was performed using the bootstrap technique. Each variable was assigned a score on a scale ranging from 0 to 100, and the total score was calculated by summing the individual scores.[17] The predictive accuracy of the model was assessed using the receiver operating characteristic (ROC) curve and the calibration curve (CC). Furthermore, decision curve analysis (DCA) and clinical impact curve (CIC) were utilized to evaluate the practical application and clinical relevance of the predictive model.

Results

Data Collection

A cohort of 548 elderly patients with diabetes and CKD stage 5 was included in the study, all patients successfully underwent the surgical procedure. After a 12-week surveillance period post-AVF surgery, patients were dichotomized into two distinct cohorts based on their AVF maturity status. Specifically, 386 patients, comprising 70.44% of the entire cohort, were categorized into the mature AVF group, whereas the remaining 162 patients, accounting for 29.56%, were assigned to the immature AVF group. A detailed flowchart illustrating the systematic patient selection process is presented in Figure 1.

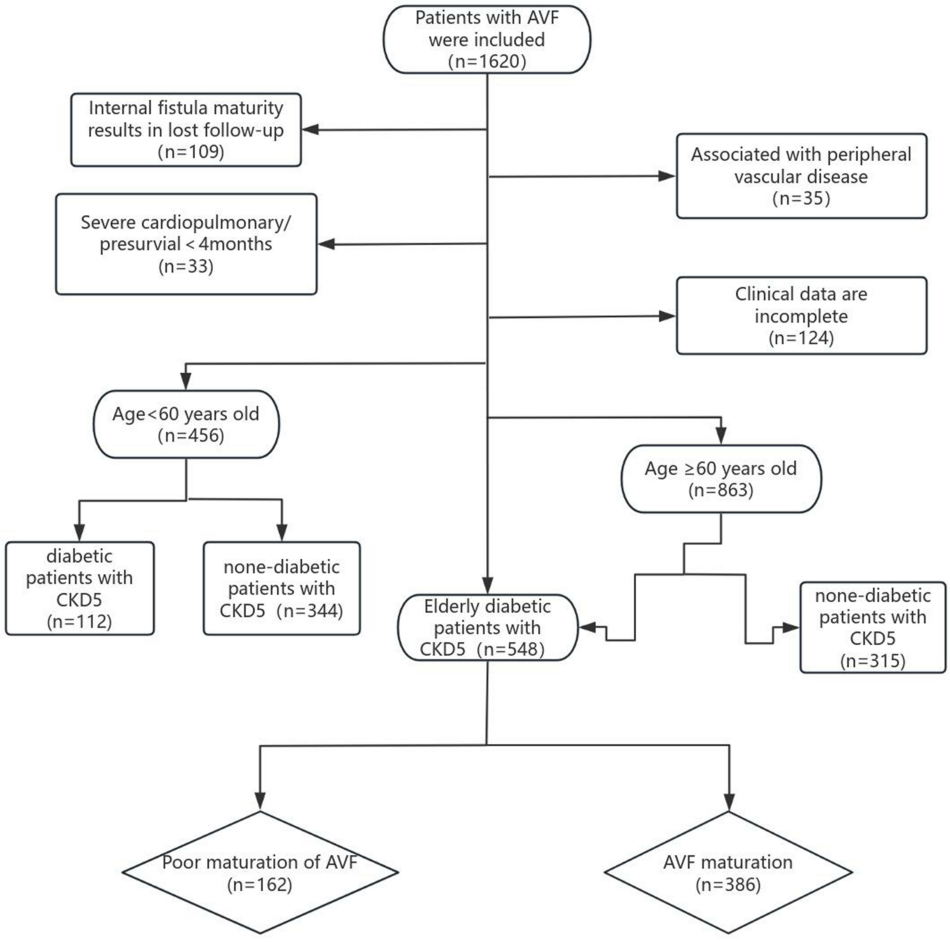

Figure 1 AVF patients selection process.

Selection of Predictor Variables

A Comparative Analysis Was Conducted to Assess the Demographic Characteristics of Patients in Both the Mature and Immature AVF Groups

The statistical evaluation revealed no significant differences in factors such as age, BMI, gender, smoking history, CVD, and hypertension (all P-values ≥ 0.05). However, a statistically significant divergence was observed in the history of CVIN procedures (P < 0.05). These results are succinctly summarized in Table 1.

A Comparative Assessment of Biochemical Parameters Was Performed Between the Mature and Immature AVF Groups

The analysis demonstrated no statistically significant variations in the distribution ranges of WBC, PLT, NEU, LYM, RDW, HB, FDP, ALB, SCR, BUN, TG, FBG, PTH, PCT, CRP, ESR, NLR, PLR, PAR, PNI, and TYG (all P-values ≥ 0.05). Conversely, statistically significant differences were identified in the levels of RBC, D-D, BUA, Pro-BNP, LDL and TC (P < 0.05). These findings are detailed in Table 2.

A Comparative Analysis of the Mature and Immature AVF Groups Showed No Statistically Significant Difference in LVEF (P ≥ 0.05)

However, significant statistical disparities were observed in IRM, ICVM, and the presence of RAP, as outlined in Table 3

The Univariate Combined With Lasso Regression Screened Potential Predictors

RBC, D-D, BUN, Pro-BNP, LDL, TC, IRM, ICVM, RAP, and CVIN, all of which displayed statistical significance (P<0.05). Following a comprehensive LASSO regression analysis on the training cohort, the initial set of potential predictors was narrowed down to five. The coefficients for these five predictors are detailed in Table 4, while Figure 2 visually represents their profiles. Additionally, Figure 3 illustrates the cross-validated error plot for the LASSO regression model. By utilizing regularization techniques, the final model integrated these five variables, maintaining the cross-validated error within one standard error of the minimum. Subsequent multivariate logistic analyses were conducted on distinct cohorts, with the detailed results presented in Table 5.

Development of a Nomogram for Predicting the Maturation Status of AVF

Drawing upon clinical expertise and acknowledging the potential correlation of these indices with AVF immaturity, all five indices were incorporated into a multivariate logistic regression analysis. Subsequently, the backward stepwise regression approach was utilized to achieve an optimal equilibrium between model complexity and data fitting. Ultimately, all five indices were retained in the predictive model, yielding an Akaike Information Criterion (AIC) value of 350.13. Upon removal of CVIN, RAP, DD, LDL and RAP, the remaining four variables were incorporated into the predictive model, with their respective AIC values being 378.85, 379.86, 490.17, 356.64, and 367.62. Based on the AIC values, the decision was made to include all five indices in the final predictive model. The definitive logistic model, comprising five independent predictors (D-D, LDL, IRM, RAP, and CVIN), has been transformed into an intuitive nomogram, as depicted in the subsequent figure (Figure 4). This nomogram utilizes equations to determine the total

Table 1 Demographic Characteristics of the AVF Mature Group and Immature Group

Variables	Total (n = 548)	Mature Group (n = 387)	Immature Group (n = 161)	Statistic	*P*
Age (years)	65.00 (62.00, 70.00)	65.00 (62.00, 70.00)	65.00 (62.00, 70.00)	Z=−0.14	0.889
BMI (kg/m^2)	23.48 (20.80, 26.10)	23.50 (20.90, 26.30)	23.20 (20.70, 25.16)	Z=−1.56	0.119
Male n (%)	387 (70.62)	266 (68.73)	121 (75.16)	χ^2=2.26	0.133
Smoke n (%)	186 (33.94)	132 (34.11)	54 (33.54)	χ^2=0.02	0.898
CVD (%)	194 (35.40)	133 (34.37)	61 (37.89)	χ^2=0.62	0.432
Hypertension n (%)	492 (89.78)	350 (90.44)	142 (88.20)	χ^2=0.62	0.430
CVIN n (%)	61 (11.13)	13 (3.36)	48 (29.81)	χ^2=80.44	<0.001*

Notes: *indicates that there is a statistical difference between the AVF mature group and the AVF immature group. *P < 0.05 indicated statistical significance.

Abbreviations: BMI, Body mass index; CVD, Cardiovascular and cerebrovascular diseases; CVIN, Cephalic vein indwelling needle.

Table 2 Biochemical Indicators of the AVF Mature Group and Immature Group

Variables	Total (n = 548)	Mature Group (n = 387)	Immature Group (n = 161)	Statistic	*P*
RBC (10*12/L)	3.10 (2.69, 3.54)	3.07 (2.67, 3.50)	3.25 (2.73, 3.68)	Z=−2.54	0.011*
WBC (10*9/L)	6.17 (5.20, 7.56)	6.15 (5.21, 7.30)	6.34 (5.19, 7.73)	Z=−0.30	0.768
PLT (10*9/L)	188.50 (145.00, 239.00)	186.00 (147.00, 234.00)	197.00 (141.40, 269.00)	Z=−1.19	0.236
NEU (10*9/L)	4.12 (3.30, 5.30)	4.11 (3.34, 5.22)	4.17 (3.14, 5.35)	Z=−0.80	0.426
LYM (10*9/L)	1.24 (0.91, 1.56)	1.23 (0.90, 1.56)	1.36 (0.98, 1.52)	Z=−1.39	0.166
RDW (f L)	46.50 (43.06, 50.00)	46.30 (43.09, 49.90)	46.70 (42.81, 50.39)	Z=−0.68	0.496
Hb (g/L)	89.00 (78.00, 105.00)	89.00 (77.60, 104.50)	92.00 (80.00, 108.00)	Z=−1.63	0.104
D-D (mg/dL)	1.37 (0.67, 2.99)	0.98 (0.54, 1.79)	3.50 (1.63, 5.49)	Z=−12.82	<0.001*
FDP (mg/dL)	3.81 (3.24, 4.57)	3.82 (3.25, 4.73)	3.81 (3.16, 4.34)	Z=−1.82	0.069
ALB (g/L)	34.40 (30.60, 38.68)	34.39 (30.40, 38.05)	34.58 (30.80, 40.09)	Z=−1.30	0.195
SCR (u mol/L)	591.65 (447.35, 786.90)	597.00 (450.25, 771.95)	577.70 (439.70, 790.30)	Z=−0.44	0.659
BUN (mmol/L)	16.84 (11.95, 24.17)	17.13 (11.88, 23.95)	16.81 (12.69, 24.27)	Z=−0.36	0.720
BUA (u mol/L)	341.28 (249.97, 425.65)	347.70 (256.00, 432.05)	311.70 (230.34, 413.20)	Z=−2.08	0.037*
Pro-BNP (uh/L)	1854.50 (591.25, 11,690.50)	1522.00 (536.00, 6893.50)	3910.00 (737.00, 24,030.00)	Z=−3.05	0.002*
TG (mmol/L)	1.45 (1.06, 1.85)	1.46 (1.06, 1.85)	1.44 (1.01, 1.96)	Z=−0.10	0.923
LDL (mmol/L)	2.51 (2.01, 3.18)	2.40 (1.88, 2.93)	2.91 (2.31, 3.61)	Z=−6.71	<0.001*
TC (mmol/L)	4.33 (3.47, 5.26)	4.40 (3.64, 5.31)	4.13 (3.32, 5.15)	Z=−2.80	0.005*
FBG (mmol/L)	5.51 (4.80, 6.91)	5.50 (4.82, 6.82)	5.53 (4.65, 7.11)	Z=−0.19	0.851
PTH (p mol/L)	334.50 (202.75, 524.00)	330.00 (203.50, 520.00)	370.00 (200.00, 544.00)	Z=−1.00	0.320
PCT (ng/mL)	0.35 (0.17, 0.65)	0.32 (0.15, 0.66)	0.37 (0.21, 0.63)	Z=−1.26	0.206
CRP (mg/L)	9.00 (4.93, 17.38)	8.48 (4.62, 16.69)	11.43 (5.48, 19.10)	Z=−1.50	0.134
ESR (mmol/h)	49.00 (31.00, 72.00)	48.00 (31.00, 71.00)	52.00 (31.00, 74.00)	Z=−0.54	0.590
NLR	3.39 (2.41, 4.74)	3.44 (2.45, 4.86)	3.09 (2.17, 4.57)	Z=−1.92	0.055
PLR	152.92 (109.39, 215.56)	151.95 (110.95, 216.85)	169.54 (107.86, 207.07)	Z=−0.01	0.991
PAR	5.46 (4.26, 7.19)	5.45 (4.32, 7.10)	5.60 (4.02, 7.78)	Z=−0.58	0.559
PNI	41.00 (36.40, 45.20)	40.90 (36.25, 44.67)	41.28 (36.95, 46.80)	Z=−1.50	0.133
TYG	4.75 (4.55, 4.94)	4.76 (4.56, 4.93)	4.73 (4.54, 4.98)	Z=−0.40	0.686

Notes: *indicates that there is a statistical difference between the AVF mature group and the AVF immature group. *P < 0.05 indicated statistical significance.
Abbreviations: RBC, Red blood cell count; WBC, White blood cell count; PLT, Platelet count; NEU, Neutrophil count; LYM, Lymphocyte count; RDW, Erythrocyte distribution width; HB, Hemoglobin; D-D, D - dimer; FDP, Fibrinogen degradation products; ALB, Albumin; SCR, Serum creatinine; BUN, Blood urea nitrogen; BUA, Blood uric acid; Pro-BNP, Precursor-Brain natriuretic peptide; TG, Yriglyceride; LDL, Low-density lipoprotein; TC, Total cholesterol; FBG, Fasting plasma glucose; PTH, Parathyroid hormone; PCT, Procalcitonin; CRP, C-reactive protein; ESR, Erythrocyte sedimentation rate; NLR, Neutrophil lymphocyte ratio; PLR, Platelet lymphocyte ratio; PAR, Platelet albumin ratio; PNI, Prognostic nutritional index=ALB (g/L)+5*LYM(10*9/L); TYG, Triglyceride glucose index=ln [TG (mg/dl) * FBG (mg/dl)]/2.

Table 3 Imaging Indicators of the AVF Mature Group and Immature Group

Variables	Total (n = 548)	Mature Group (n = 387)	Immature Group (n = 161)	Statistic	*P*
IRM (mm)	2.30 (2.00, 2.60)	2.40 (2.10, 2.60)	2.00 (1.80, 2.40)	Z=−8.35	<0.001*
ICVM (mm)	2.30 (1.90, 2.70)	2.40 (2.10, 2.80)	1.90 (1.50, 2.40)	Z=−8.10	<0.001*
LVEF (%)	63.00 (59.00, 67.00)	63.00 (59.00, 67.00)	63.00 (60.00, 66.00)	Z=−0.43	0.665
RAP n (%)	76 (13.87)	18 (4.65)	58 (36.02)	χ^2=93.69	<0.001*

Notes: *indicates that there is a statistical difference between the AVF mature group and the AVF immature group. *P < 0.05 indicated statistical significance.
Abbreviations: LVEF, Left ventricular ejection fraction; IRM, Internal radial meridian; ICVM, Internal cephalic vein meridian; RAP, Radial artery plaque.

points for each patient, calculated as follows: Points = 5 × D-D (mg/dL) + 3.12 × LDL (mmol/L) + 71–9.38 × IRM (mm) + [RAP (0=0 points; 1=14.8 points)] + [CVIN (0=0 points; 1=15.9 points)]. For instance, a patient with a DD of 5.78 mg/dL, LDL of 3.25 mmol/L, IRM of 1.7 mm, absence of RAP, and a history of CVIN would receive a total score of 110 points, corresponding to a 98.6% probability of having an immature AVF. These details are outlined in Figure 5. Given

Table 4 The Coefficients of Lasso Regression Analysis

Variables	Coefficient
Intercept	−1.12845554
DD (mg/dL)	0.29904655
LDL (mmol/L)	0.01201556
IRM (mm)	−0.40573961
RAP n (%)	0.99498047
CVIN n (%)	0.87552156

that this patient falls into the high-risk category, they would benefit from preventive measures, such as lipid-lowering therapies.

Evaluation of Predictive Models

Assessment and Internal Validation of the Predictive Model's Effectiveness

To ascertain the discriminatory capability of the nomogram, a ROC curve was plotted, and the AUC was determined. The nomogram for predicting immature AVF exhibited an AUC value of 0.922 (95% CI: 0.870 to 0.947). The optimal threshold provided a sensitivity of 79.5% and a specificity of 93.0% (Figure 6A). For internal validation, the bootstrap technique with 1000 resamples was applied, yielding an AUC value of 0.912 (95% CI: 0.900 to 0.935). The optimal threshold achieved a sensitivity of 77.9% and a specificity of 92.8% (Figure 6B). These findings underscore the model's exceptional ability to differentiate between elderly diabetics with varying stages of AVF maturation.

Evaluation and Internal Validation of Predictive Model Stability

The Hosmer-Lemeshow goodness-of-fit test confirmed the absence of a statistically significant difference between the predicted incidence of AVF maturation and the observed occurrence probability (χ^2=11.718, P=0.169). This outcome indicates that the model successfully passed the test, demonstrating its robust fit as there is no notable divergence between predicted and actual values (Figure 7A). Additionally, internal calibration of the model using the bootstrap

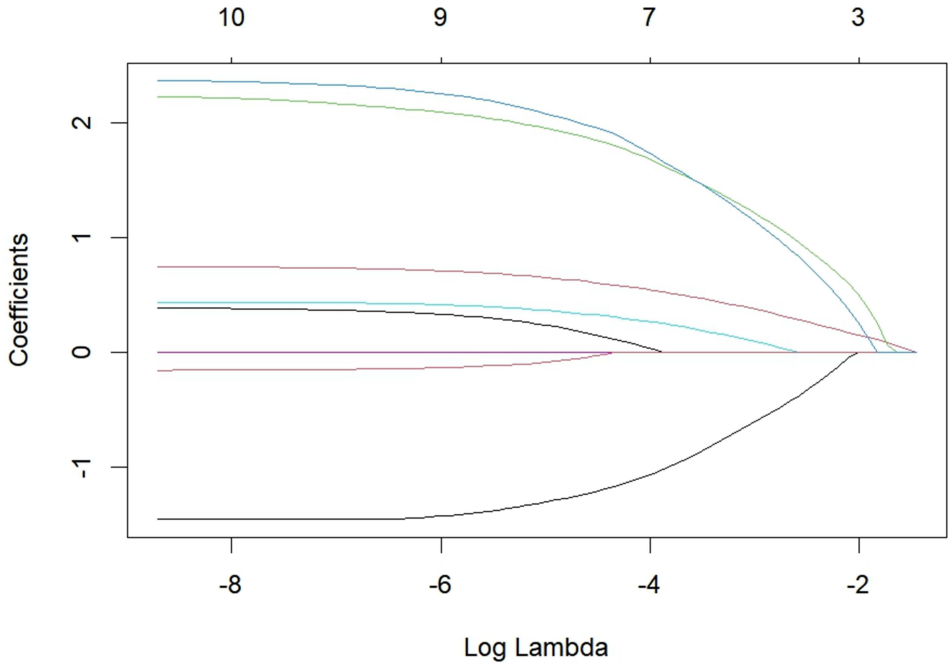

Figure 2 Lasso regression coefficient path.

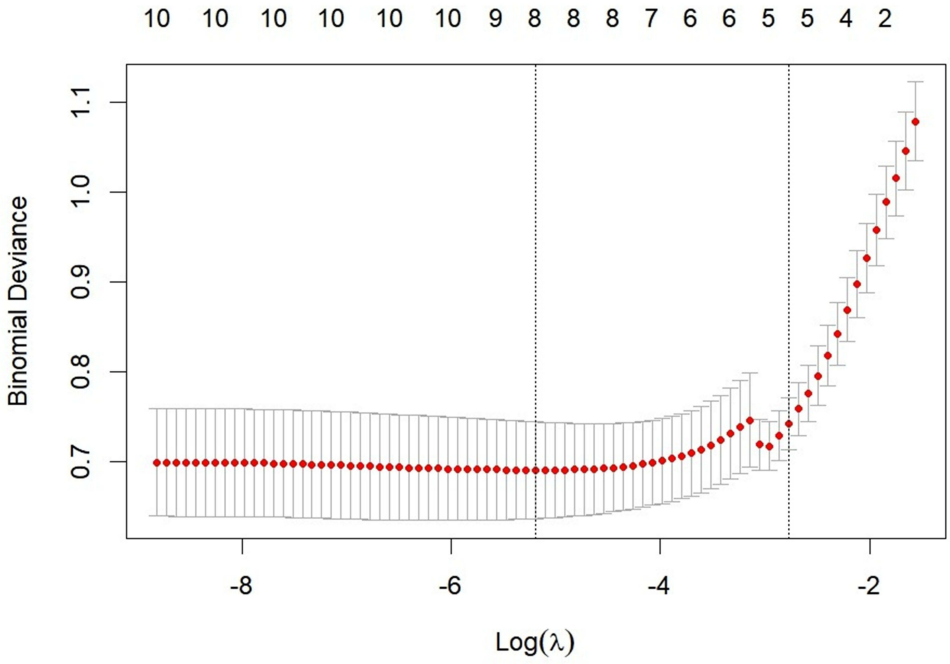

Figure 3 Lasso regression cross-validation plot.

method with 1000 resamples revealed that the CC of the predicted model closely approximates the actual curve and observed occurrence probability (χ^2=6.380, P=0.605). This further substantiates the model's capacity to provide consistent and accurate predictions of the risk of impaired AVF maturation (Figure 7B).

Assessment and Internal Confirmation of the Clinical Applicability of Predictive Models

(1) DCA was conducted on the predictive nomogram (depicted in Figure 8A). Furthermore, the model underwent internal validation through the application of the bootstrap method with 1000 resamples (illustrated in Figure 8B). The results consistently indicate that the use of the nomogram for forecasting immature AVF offers potential clinical benefits compared to strategies that universally include or exclude all patients for intervention.

(2) CICs were derived from the predictive nomogram (displayed in Figure 9A). Additionally, internal validation of the model was performed using the bootstrap method with 1000 resamples (shown in Figure 9B). These findings consistently emphasize that the nomogram's predictions for immature AVF yield a superior net clinical benefit.

Table 5 Results of Multivariate Regression Analysis

Variables	Beta	S E	Z	P	OR (95% CI)
Intercept	−1.01	0.99	−1.02	0.309	0.37 (0.05 ~ 2.54)
D-D (mg/dL)	0.73	0.08	9.04	<0.001*	2.08 (1.78 ~ 2.44)
LDL (mmol/L)	0.45	0.15	2.91	0.004*	1.57 (1.16 ~ 2.12)
IRM (mm)	−1.56	0.37	−4.19	<0.001*	0.21 (0.10 ~ 0.44)
RAP n (%)	2.12	0.39	5.45	<0.001*	8.31 (3.88 ~ 17.79)
CVIN n (%)	2.25	0.43	5.20	<0.001*	9.44 (4.05 ~ 22.01)

Notes: *indicates that there is a statistical difference between the AVF mature group and the AVF immature group. *P < 0.05 indicated statistical significance.
Abbreviations: D-D, Plasma D - dimer; LDL, Low-density lipoprotein; IRM, Internal radial meridian; RAP, Radial artery plaque; CVIN, Cephalic vein indwelling needle.

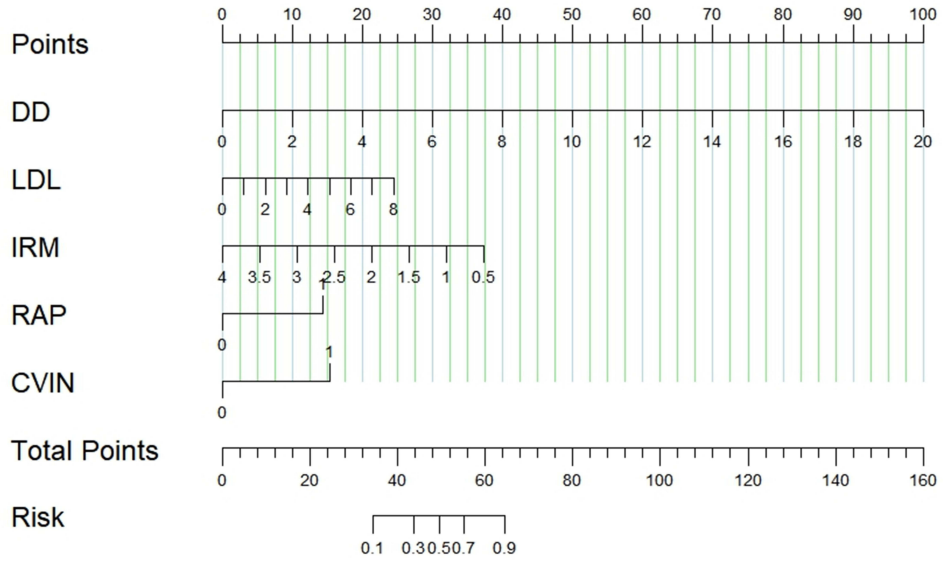

Figure 4 The nomogram for predicting immature AVF based on the elderly diabetics (n = 548).

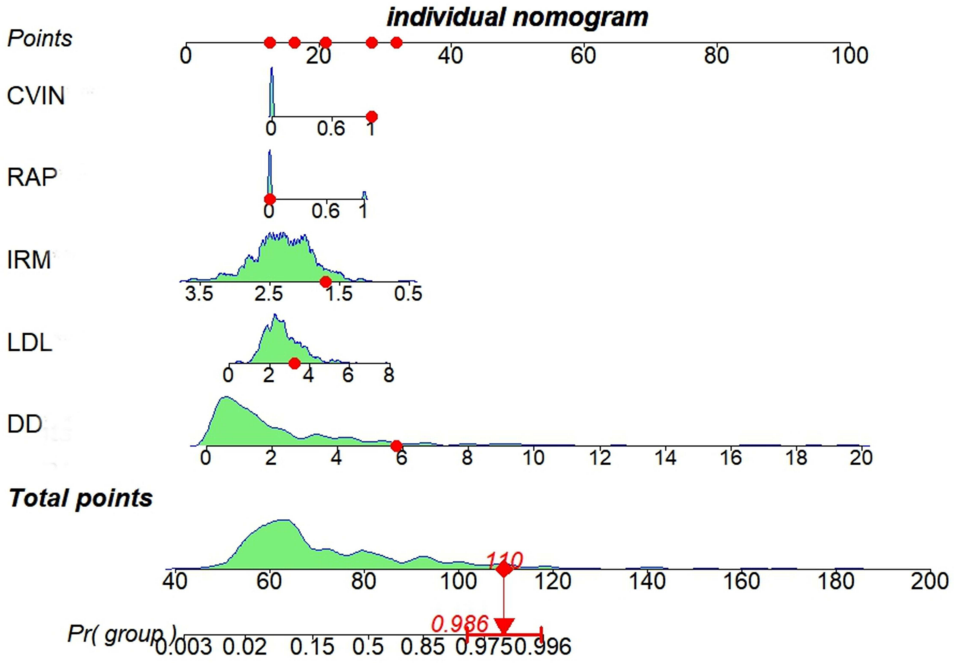

Figure 5 The individual nomogram (on the web) for predicting immature AVF.

Discussion

This study has developed a predictive model utilizing five easily accessible measures, marking the first instance, to our knowledge, of evaluating immature AVF in elderly adults with diabetes through a nomogram model. The originality of our findings stems from the unprecedented discovery and examination of the influence of CVIN on AVF maturation, as well as its predictive value in identifying immature AVF. The diagnostic map, encompassing D-D, LDL, IRM, RAP, and CVIN, accurately and discriminatively anticipated AVF maturation. With an AUC of 0.922 (95% CI, 0.897 to 0.947), the prediction models exhibited excellent differentiation. Through internal validation utilizing the bootstrap technique, replicated 1000 times, it was ascertained that the calibration curve closely approximated the ideal curve, indicating

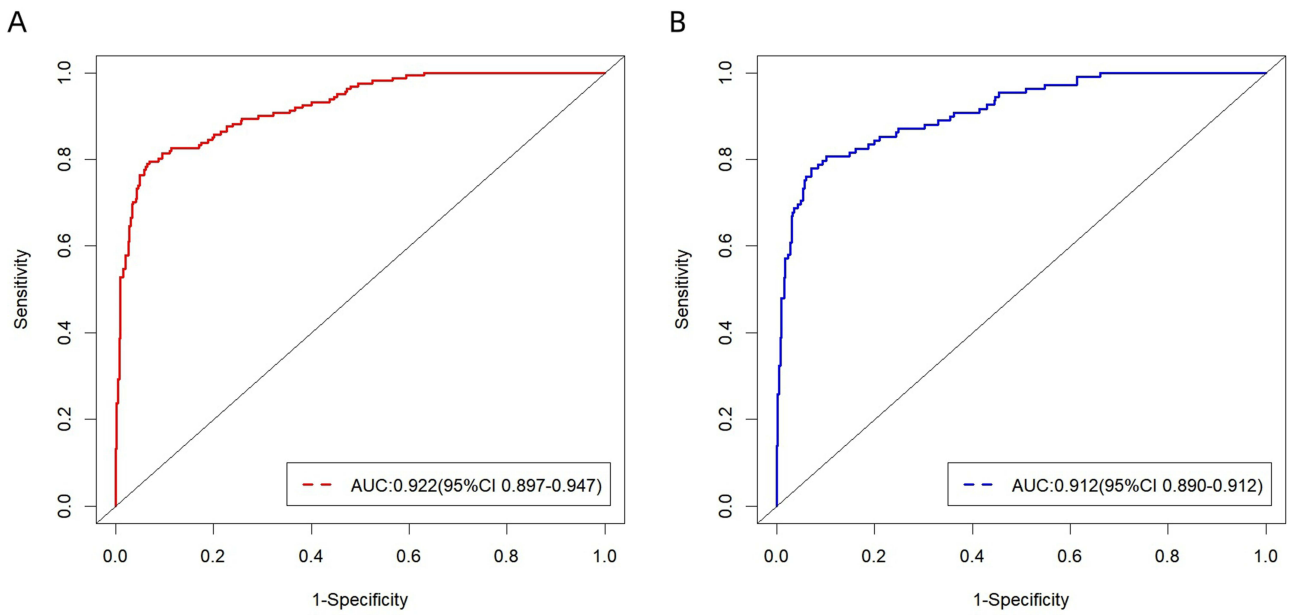

Figure 6 (A): Diagnostic efficacy of predictive models in the training cohort; (**B**): Diagnostic efficacy of predictive models in the internal validation cohorts.

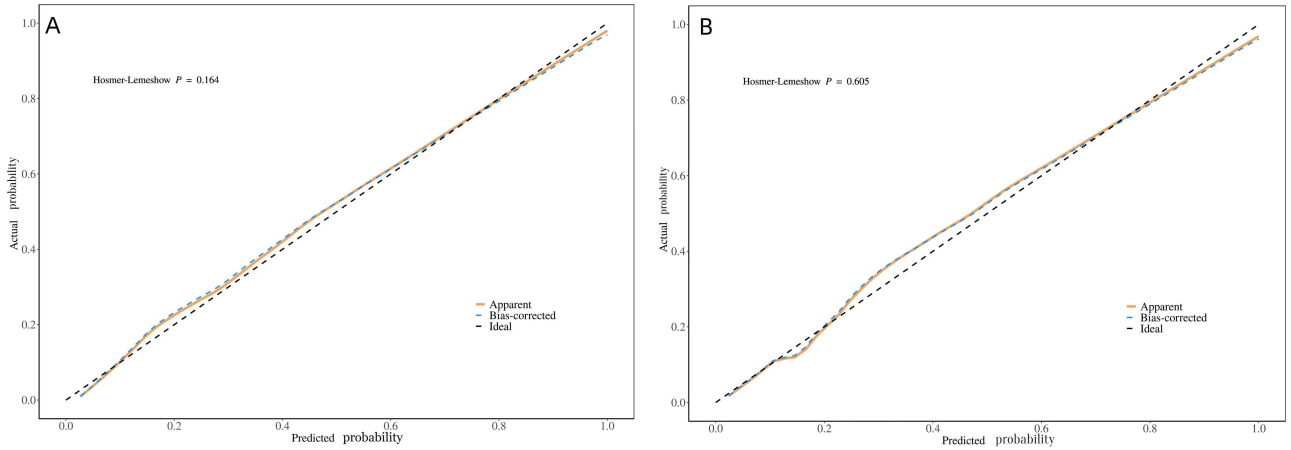

Figure 7 (**A**): The calibration curves for predicting immature AVF in the training cohort; (**B**): The calibration curves for predicting immature AVF in the internal validation cohorts.

a slope proximal to unity. Consequently, the predicted risk of maturation aligned closely with the actual risk. The Hosmer-Lemeshow goodness-of-fit test yielded a χ^2 value of 11.718 with a P-value of 0.167, suggesting an acceptable level of agreement in predicting the maturation of AVF. Furthermore, this study employed the DCA and CIC evaluation models to comprehensively assess the clinical utility of the nomogram, by comparing the clinical benefits of targeted interventions with those of no interventions across the entire patient cohort. The DCA and CIC analysis confirmed the nomogram's clinical net benefit in predicting immature AVF among elderly diabetics. Overall, this nomogram prediction model, based on independent risk factors for immature AVF, enables individualized risk assessment in elderly diabetics.

Current Status and Influencing Factors Contributing to Impaired AVF Maturation in Elderly Diabetics

The maturation process of AVF involves intricate vascular remodeling. Following AVF anastomosis, blood flow experiences a significant surge, leading to increased vascular pressure. This prompts compensatory vascular remodeling

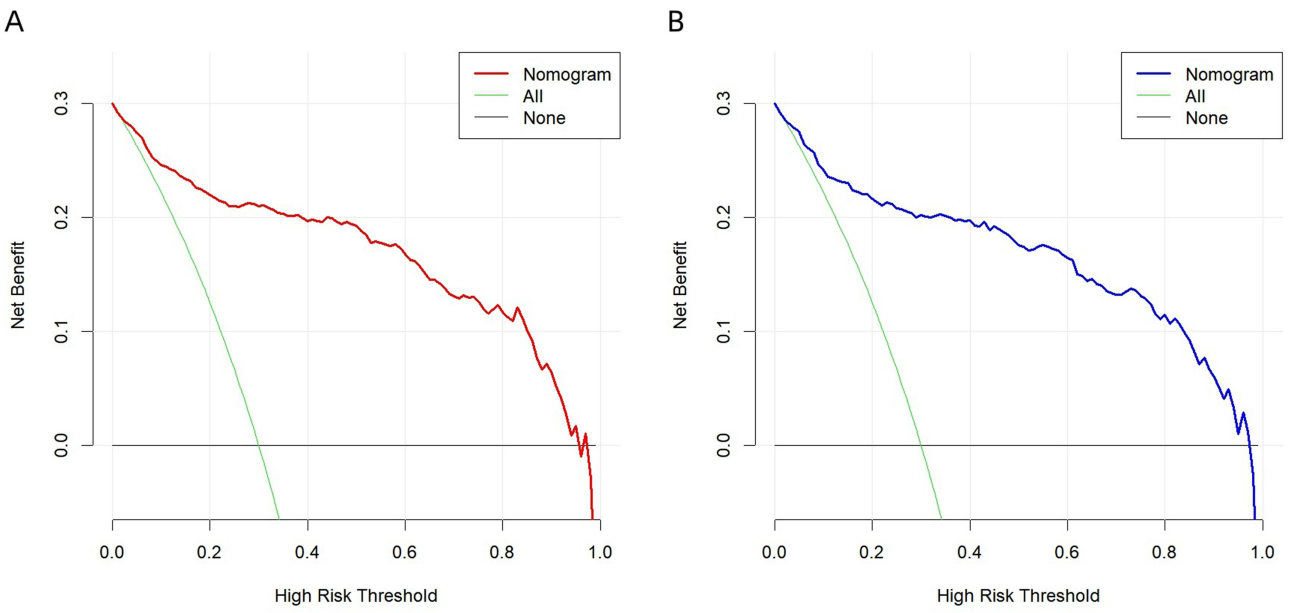

Figure 8 (**A**): DCA analysis for the proposed nomogram model in the training cohort. The Y-axis shows the net benefit. The green line represents the assumption that all patients have the immature AVF and accept treatment. The black line represents the assumption that no patients have the immature AVF and not accept treatment. The red line represents the nomogram. The decision curve in indicated that if the threshold probability is between 0 and 1.0, then using the nomogram to predict the immature AVF adds more benefit than the treat-all patients scheme or treat-none scheme. (**B**). DCA analysis for the proposed nomogram model in the internal validation cohorts. The Y-axis shows the net benefit. The green line represents the assumption that all patients have the immature AVF and accept treatment. The black line represents the assumption that no patients have the immature AVF and not accept treatment. The blue line represents the nomogram. The decision curve in indicated that if the threshold probability is between 0 and 1.0, then using the nomogram to predict the immature AVF adds more benefit than the treat-all patients scheme or treat-none scheme.

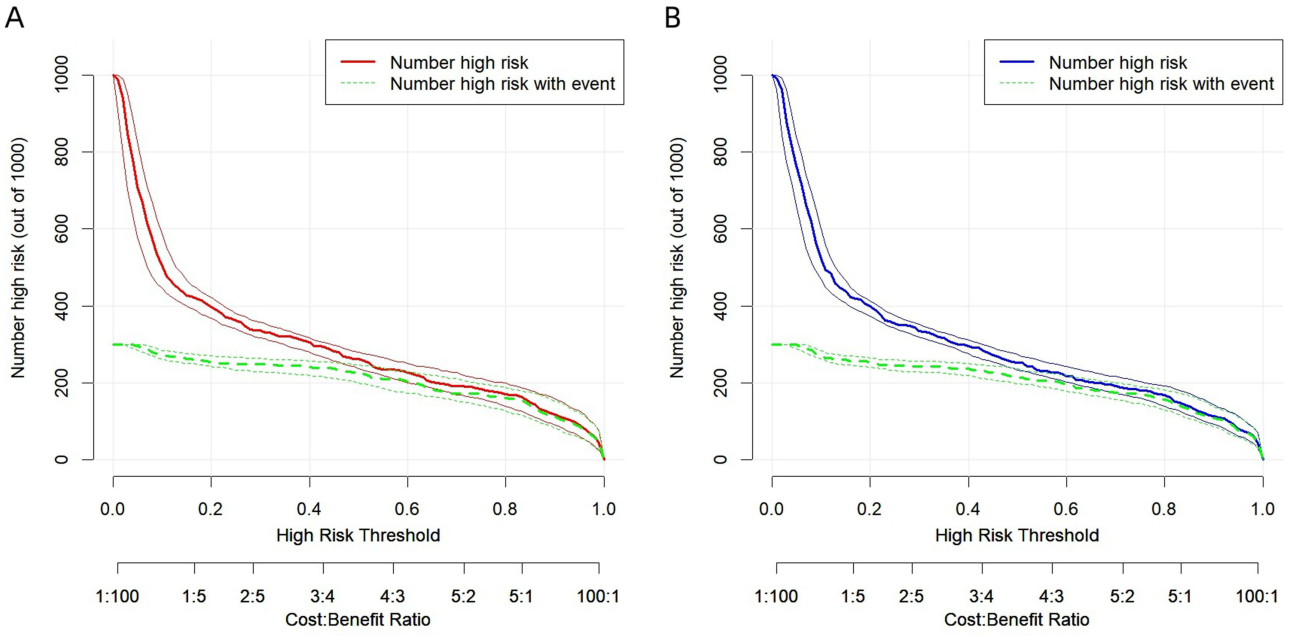

Figure 9 (**A**): CIC of nomogram model in the training cohort. The red cure (number of high-risk individuals) indicates the number of people who are classified as positive (high risk) by the model at each threshold probability; the green curve (number of high-risk individuals with outcome) is the number of true positives at each threshold probability. CIC visually indicated that nomogram conferred high clinical net benefit and confirmed the clinical value of the nomogram model. (**B**): CIC of nomogram model in the internal validation cohorts. The blue cure (number of high-risk individuals) indicates the number of people who are classified as positive (high risk) by the model at each threshold probability; the green curve (number of high-risk individuals with outcome) is the number of true positives at each threshold probability. CIC visually indicated that nomogram conferred high clinical net benefit and confirmed the clinical value of the nomogram model.

within the vessel wall, encompassing endothelial and matrix remodeling, ultimately fostering a conducive blood flow environment for MHD. If the AVF fails to achieve adequate maturity, it results in insufficient blood flow to fulfill the requirements of MHD. While existing studies have explored complications associated with AVF in MHD patients, such as failure, loss of patency at 5/10 years, stenosis, thrombosis and impaired maturation, large-scale data analysis has yet to reveal the incidence of immature AVF specifically among elderly diabetes individuals. Furthermore, clinical research focusing on the risk factors underpinning immature AVF remains scant. In this investigation, we observed a 29.56% incidence of impaired AVF maturation in elderly diabetics, exceeding the 21% reported by Bylsma et al.[2] A cohort study conducted by Zi-Ming Wan et al[28] revealed age as a significant risk factor for compromised AVF maturation, with the risk escalating by over 1.54 times for every 20-year increment in age. Clinically, it has been observed that the rate of immature AVF is notably higher in patients with diabetes and CKD stage 5 compared to non- diabetes cohorts.[3] This disparity may be attributed to the gradual thickening of the intima-media with advancing age, compounded by a heightened risk of endothelial damage, stenosis and obstruction arising from vascular diseases.[10,29] Notably, in diabetics, excessive advanced glycosylation end products interact with their respective receptors, triggering vascular inflammation, fibrosis, and pro-coagulation reactions. This cascade of events results in blood vessel narrowing and endothelial dysfunction, thereby hindering AVF maturation.[12–14]

Based on our findings, the independent risk factors for impaired AVF maturation in elderly diabetics include, but are not limited to, the aforementioned factors. D-D Level: Elevated FIB, as an acute-phase reactive protein, is typically observed in scenarios conducive to hemostasis, platelet aggregation, and alterations in blood vessel walls. D-D, the principal degraded fragment of FIB, serves as compelling evidence of acute thrombosis and also acts as an indicator of persistent thrombus status. This study's findings suggest that an increase in D-D levels negatively impacts the immature maturation of AVF. Research has demonstrated that vascular stenosis and the resultant thrombosis can lead to decreased blood flow and abnormal vascular remodeling, both of which are prevalent complications associated with inadequate AVF maturation.[30–32] However, the intricate interplay between D-D levels and AVF immaturity remains incompletely understood. LDL Level: Abnormal lipid metabolism is a prevalent complication among patients with ESRD. Enhanced blood viscosity and lipid deposition on the inner walls of blood vessels heighten the risk of atherosclerosis, with LDL being a pivotal risk factor for the development of atherosclerotic pathology.[33,34] The fundamental state of blood vessels can influence the maturation process of AVF. This study's results indicate that elevated LDL levels are associated with a greater risk of impeded AVF maturation, consonant with prior reports.[35,36]

IRM: IRM plays a critical role in the development of AVF as they mature. However, there remains a lack of consensus regarding the minimum vascular diameter required for a successful creation of AVF. The European Vascular Access Guidelines and the Kidney Disease Outcomes Quality Initiative Guidelines both stress the importance of carefully evaluating or deselecting surgical sites in patients with stage 5 CKD, especially when the radial or cephalic vein diameters are below 2.0 mm. In contrast, the Japanese vascular access guidelines offer more specific criteria, indicating that the radial artery should have an internal diameter between 1.5 mm and 2.0 mm, while the vein should have a diameter between 1.6 mm and 2.5 mm after applying a tourniquet. Success rates of surgeries tend to decrease when these recommended thresholds are not met. Considering the unique characteristics of the Chinese population and the practical challenges in patient care, experts generally agree that a preoperative radial artery and cephalic vein diameter of at least 2.0 mm (post-tourniquet application) can serve as a reliable indicator for surgical intervention.[37] These study findings are consistent with previous research, which highlights a positive relationship between IRM and the maturation of AVF. This emphasizes the importance of assessing vascular diameter in the preoperative phase and during surgical planning.[38–40] RAP: Arterial calcification is a prevalent problem affecting approximately 20%~40% of end-stage renal disease patients, especially in the elderly and those with diabetes. This calcification of the arteries poses a significant challenge to the successful development and improvement of AVF, potentially hindering their proper maturation.[41] While ultrasound imaging can detect and measure arterial wall calcification, there is currently no standardized grading system for evaluating calcification in the upper limb arteries. The guidelines established by the American Institute of Ultrasound in Medicine for vascular mapping only require the identification and documentation of calcification, without specific grading criteria.[42] The existing literature on AVF in patients with extensive radial artery calcification is limited. Therefore, in our study, the degree of radial artery calcification was not graded, and the type included in this index

was only a binary variable rather than a grade variable. However, for patients with positive Allen test before surgery, severe calcification, sclerosis of the radial artery, and lumen stenosis, we excluded the operation. This research indicates that radial artery calcification has a negative impact on AVF maturation, consistent with previous studies.[43,44] However, some research has suggested that there is no significant difference in AVF maturity, both clinically and based on imaging, between patients with mild calcification and those without, despite a moderate decrease in fistula blood flow.[45] A retrospective analysis of 741 patients discovered that 100 out of 166 diabetics displayed arteriosclerosis, with only about 10% showing immature AVF. This indicates that arteriosclerosis and plaque-related changes, especially in type II diabetes patients, may not significantly impede AVF maturation. Instead, the study highlights that damage to the veins due to repeated fluid administration before dialysis is the primary obstacle to AVF maturation.[46] Thus, further research into the effects of radial artery calcification on AVF maturation is essential, particularly through large-scale prospective studies. CVIN: Multivariate analyses have consistently revealed that the diameter and dilation of the cephalic vein are pivotal factors in the maturation process of AVF.[47–49] Specifically, cephalic veins with a diameter of 2 mm or greater and venous dilation of at least 0.5 mm are associated with a higher likelihood of AVF maturity.[50] Conversely, a cephalic vein diameter below 2 mm may adversely impact the successful maturation rate of AVF,[51] posing a potential risk for AVF maturation failure. Additionally, the findings of this study indicate that a previous history of CVIN is a risk factor for impaired AVF maturation in elderly diabetics.

Notably, there has been a lack of clinical research exploring the correlation between a history of catheters in the cephalic vein and AVF maturation. It is hypothesized that due to the frequent need for fluid rehydration in patients, long-term and repeated use of intravenous indentation needles may lead to a certain degree of cephalic vein injury, affecting its dilation and potentially compromising AVF maturation. This perspective aligns with the views expressed in the study conducted by Gołębiowski et al.[46] In a retrospective study involving 189 patients, Engin et al[52] demonstrated that the TYG index served as an independent predictor of primary AVF failure among diabetic patients. Conversely, our findings revealed no statistically significant difference in the TYG index between the mature AVF group and the immature AVF group within the elderly diabetic cohort.

Summary and Limitations

After a thorough evaluation incorporating D-D, LDL, IRM, RAP, and CVIN, the nomogram model developed for assessing the risk of AVF maturation in elderly diabetics demonstrates impressive discriminatory ability, consistency, and practical applicability in a clinical setting. In clinical practice, it is imperative to reinforce preventative measures tailored to individual patients' risk profiles for immature AVF. This tailored approach enhances the relevance and efficacy of preventative measures, offering valuable guidance for the establishment and maintenance of AVF in this patient population. However, this study is not without its limitations. Firstly, this study is characterized by being a single-center, retrospective analysis with a relatively modest sample size. Consequently, certain indicators that could have enhanced the study's comprehensiveness, such as glycosylated hemoglobin levels and urinary protein concentrations, were not incorporated, potentially introducing selection bias. Secondly, although we created a nomogram model for risk prediction, our variable selection process solely relied on statistical significance ($p<0.05$) derived from logistic regression analysis. It should be noted that $p<0.05$ is not an absolute criterion for variable inclusion in predictive models. Similarly, while the impact of ICVM on AVF maturity is well-documented in the literature, its significance in our multivariate regression analysis was not evident, possibly due to the small sample size. The model has not yet stratified the elderly population according to age, resulting in uncertainty regarding its predictive value across different elderly age groups. Furthermore, as a single-center study, the nomogram model lacks external validation, limiting its generalizability. For future research endeavors, it is imperative to utilize larger sample sizes, foster multicenter collaborations, and conduct prospective data analyses in order to bolster the clinical relevance and applicability of the prediction model.

Conclusion

In this study, we have developed a novel nomogram model for predicting the risk of immature AVF in elderly diabetics utilizing AVF as their dialysis access. This model incorporates five key detection indicators, including D-D, LDL, IRM, RAP, and CVIN, to effectively forecast the occurrence of immature AVF. This predictive model offers medical personnel

a straightforward and highly accurate visual tool for identifying patients at risk of immature AVF at an early stage, enabling timely intervention.

Data Sharing Statement

Upon receipt of a valid request, the datasets employed in this research can be obtained from the corresponding author.

Informed Consent

Given the retrospective nature of our study, the Ethics Committee of Baoding First Central Hospital, Hebei Medical University, granted an exemption from obtaining written informed consent. Throughout the research process, we have adhered strictly to medical ethical guidelines, ensuring compliance and respecting patients' privacy rights. Patient data is exclusively used for the purposes outlined in this research and will not be utilized for any commercial activities, advertising, or purposes unrelated to the research objectives without explicit consent from the patient or their legal representative.

Approval and Consent for Participation

The research received authorization from the Ethics Committee of Baoding First Central Hospital, affiliated with Hebei Medical University (approval number: Kuai [2023]066), and adhered strictly to the guidelines and principles outlined in the Declaration of Helsinki. Given the study's retrospective design, the Ethics Committee granted an exemption from obtaining written informed consent.

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Author Contributions

Shuangyan Liu, Yaqing Wang and Xiaojie He are first authors. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest. The research was conducted independently of any commercial or financial relationships that could be perceived as a potential conflict of interest.

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