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ORIGINAL RESEARCH

Development and Validation of a Machine Learning-Based Predictive Model for Peripheral Neuropathy Risk in Elderly Patients with Type 2 Diabetes

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Background: Diabetic peripheral neuropathy (DPN) is highly prevalent among elderly patients with type 2 diabetes; however, existing models exhibit suboptimal performance and lack specificity. This study aims to develop and validate a machine learning-based model for early identification of DPN risk.

Methods: We retrospectively collected the data of 1450 elderly patients with type 2 diabetes using the electronic medical record system of the National Metabolic Management Center (MMC) at a tertiary hospital in Shanghai's Pudong New Area from March 2022 to March 2025. The dataset included general information, disease-related indicators, and laboratory results. We randomly divided the dataset into training and testing sets in a 7:3 ratio. After feature preprocessing and selection, four machine learning algorithms—logistic regression, naïve Bayes, random forest, and extreme gradient boosting (XGBoost)—were used to construct prediction models. Hyperparameter tuning was executed through grid search combined with 5-fold cross-validation, and model performance was evaluated using the Area Under the Receiver Operating Characteristic Curve (AUC), accuracy, precision, recall, F1-score, calibration curves, and Decision Curve Analysis (DCA). The SHapley Additive exPlanations (SHAP) analysis was applied for model interpretation.

Results: The prevalence of DPN was 42.9% (623/1450). Nine variables were identified as independent predictors: diabetes duration, HbA1c, sleep quality, Charlson Comorbidity Index, sugar-sweetened beverage intake, peripheral arterial disease, sedentary behavior, smoking, and hypertension. Among the models, XGBoost performed best with an AUC of 0.951, accuracy of 0.878, precision of 0.876, recall of 0.834, F1-score of 0.855, and Brier score of 0.087. SHAP analysis confirmed the dominant contribution of diabetes duration and HbA1c to model predictions.

Conclusion: The XGBoost-based risk prediction model exhibited robust predictive performance and clinical utility for DPN in elderly patients with type 2 diabetes, offering potential for early identification of high-risk individuals and guiding targeted clinical interventions.

Keywords: machine learning, elderly, type 2 diabetes, diabetic peripheral neuropathies, predictive model

Introduction

Diabetic peripheral neuropathy (DPN) is one of the most prevalent chronic complications of type 2 diabetes mellitus (T2DM), characterized by progressive dysfunction of sensory and motor nerves. Clinically, it typically manifests as limb numbness, pain, and sensory abnormalities and represents the major antecedent of diabetic foot ulcers and lower-extremity amputation, leading to considerable disability and healthcare burden.[1] The prevalence of DPN among individuals with T2DM was estimated to be approximately 46% to 67.6%.[2,3] The burden of DPN is likely higher in older adults with T2DM, as advanced age was a well-established risk factor that can accelerate diabetes-related

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peripheral nerve degeneration.[4,5] Moreover, DPN often presents insidiously.[6] In older adults, early symptoms are frequently obscured by age-related sensory loss, cognitive impairment, and physical frailty, delaying recognition and increasing the risk of severe complications.[7] These characteristics collectively underscore the need for age-sensitive screening tools and early risk stratification strategies tailored to elderly patients with T2DM.

Despite its clinical importance, early detection of DPN remains challenging. Although nerve conduction studies represent the diagnostic gold standard, these methods are technically complex, costly, and impractical for widespread routine screening. Commonly used clinical screening tools, including the Michigan Neuropathy Screening Test and the Toronto Clinical Neuropathy Score, are simple and convenient; however, they heavily depend on patients' subjective reports and clinicians' judgment, limiting their objectivity and sensitivity for early stages. Therefore, early screening and risk management are essential for older adults with T2DM. Several risk prediction models for DPN have been developed. Traditional models for DPN have typically used moderate sample sizes, conventional clinical and laboratory variables–such as age, diabetes duration, glycemic control, and comorbidities, but have demonstrated only modest predictive performance.[8–11] In contrast, Machine learning (ML) models offer substantial advantages for modeling complex, high-dimensional clinical data and has demonstrated improved predictive performance compared with conventional statistical approaches, particularly when combined with interpretable frameworks such as SHapley Additive exPlanations (SHAP).[12] While studies in larger cohorts using ML have reported superior predictive accuracy,[13–16] these studies did not specifically focus on older adults,[8–11,13–16] a population at elevated risk. Moreover, these studies rarely incorporated lifestyle factors, such as sleep, physical activity, and dietary habits,[17–19] which are recognized as important determinants of DPN risk. Incorporating these variables into predictive models could improve early risk stratification[19] and guide personalized preventive strategies. Therefore, this study aims to develop and validate a machine learning–based predictive model for DPN in older adults with T2DM using a large real–world cohort by incorporating a comprehensive set of clinical, laboratory, and lifestyle risk factors. We will compare multiple ML algorithms to identify the optimal predictive model and apply SHAP analysis to enhance clinical interpretability, providing a clinically applicable tool for early risk stratification and targeted intervention in this vulnerable population.

Materials and Methods

Study Population

A total of 1450 elderly patients with T2DM were retrospectively enrolled in this study using a convenience sampling method. These patients were recruited from the National Standardized Metabolism Management Center (MMC) of a tertiary Grade A hospital in Shanghai and received follow-up care between March 2022 and March 2025. The inclusion criteria were as follows: 1) age≥65 years, and 2) a confirmed diagnosis of T2DM meeting the established diagnostic criteria for elderly patients.[20] The exclusion criteria included: 1) peripheral neuropathy attributable to other etiologies, including such as cervical/lumbar spondylosis, stroke, or the use of neurotoxic medications; and 2) incomplete medical records. The sample size was estimated based on a standard formula for clinical prediction model development:[21] $n = \exp\{[-0.508 + 0.259\ln(\varphi) + 0.504\ln(P) - \ln(MAPE)] / 0.544\}$, where$\varphi$represents the incidence rate of the outcome event (reported in the literature as 39.24–49.4%), P is the number of candidate predictors (assumed to be 10), and MAPE (Mean Absolute Percentage Error) was set at 0.05. This calculation yielded a required sample size of 525 to 584 participants for model development. Subsequently, the total sample was to be randomly divided into a training set and a test set at a ratio of 7:3, necessitating a final total sample size of 750 to 834 participants. To enhance the robustness of the predictive model, this study ultimately included 1450 patients. The research was approved by the hospital ethics committee (Approval No.: GLYYls2024-066). Patient consent for medical record review was waived, and all data were de-identified and coded to ensure confidentiality.

Research Variables

A self-administered questionnaire titled "Risk Factors for Peripheral Neuropathy in Elderly Patients with T2DM" was developed based on clinical expertise and previous research evidence, This questionnaire comprised 40 items across three sections: (1) General Demographic and Lifestyle Data: including gender, age, education, income, body mass index

(BMI), subcutaneous and abdominal fat area, physical activity level, sedentary behavior, sugar-sweetened beverage(SSB) intake, dietary habits, smoking and drinking, sleep patterns, and family history of diabetes; (2) Disease-Related Information: including diabetes duration, hypoglycemic treatment regimen, history of hypertension, peripheral arterial disease (PAD), diabetic complications, Charlson Comorbidity Index (CCI), and abdominal fat diagnosis; (3) Laboratory and Auxiliary Examination Data: including glycated hemoglobin (HbA1c), C-peptide, lipid profiles (total cholesterol [TC], triglycerides [TG], high-density lipoprotein cholesterol [HDL-C], low-density lipoprotein cholesterol [LDL-C]), free triiodothyronine (FT3), urinary creatinine, urinary microalbumin, 24-hour urinary protein quantification, urine albumin, white blood cell count (WBC), and hemoglobin (HB).

Operational Definitions of Key Variables:

- Sedentary behavior was defined as a daily sitting time of ≥ 6 hours.[22]
- Sugar-sweetened beverage (SSB) intake was defined as consuming SSBs (eg, carbonated soft drinks, fruit juice drinks, sweetened tea beverages) at least once per week or with a cumulative weekly volume of ≥ 500 mL.
- PAD was diagnosed by ankle-brachial index < 0.7.[23]
- Poor sleep quality was defined as meeting any of the following criteria: ≥3 weekly episodes of difficulty falling asleep (onset latency >30 min) or <6 hours of daily sleep.[24]

The diagnostic criteria for peripheral neuropathy were established in accordance with relevant clinical guidelines,[25] with diagnosis meeting any of the following:

① The presence of clinical symptoms of neuropathy (eg, pain, numbness, paresthesia) and at least one abnormal finding in five specific tests (ankle reflex, vibration sensation, pressure sensation, temperature sensation, pinprick sensation);
② For asymptomatic individuals, at least two abnormal findings among the five tests;
③ Reduced nerve conduction velocity or decreased wave amplitude.

In this study, the final determination of DPN was based on a clearly documented clinical diagnosis in the electronic medical records.

Statistical Analysis

All statistical analyses were conducted using Python software (version 3.13) with relevant packages including pandas, NumPy etc. Continuous variables were reported as mean±standard deviation or median (interquartile range), depending on their distribution. Categorical variables were summarized as frequency (percentage).

Data Preprocessing

To minimize bias from missing data, variables with a missing rate ≥30% were excluded. For variables with <30% missingness, continuous variables were handled using multiple imputation by MICE method, with five imputations and predictive mean matching for continuous variables. Whereas categorical variables were imputed using the mode. The dataset was randomly divided into training and testing sets in a 7:3 ratio with a fixed random seed (random_state = 42) for reproducibility. Within the training set, continuous variables were further standardized using Z-score transformation, and categorical variables were one-hot encoded.[26] A comprehensive preprocessing pipeline was established to ensure that the transformation rules derived from the training set were consistently utilized for the testing set, thereby averting any potential data leakage during model evaluation.

Feature Selection

In the training set, variables associated with DPN were initially screened through univariable analysis. Inter-group comparisons were conducted using the Student's *t*-test, Chi-square test, or Mann–Whitney *U*-test, as appropriate. Variables with statistical significance ($P < 0.05$) underwent further multicollinearity diagnosis (using variance inflation

factor VIF < 5 as the criterion). Ultimately, eligible variables were incorporated into a multivariate logistic regression analysis to identify independent risk factors for DPN in elderly patients with T2DM.

Model Development and Evaluation

Prediction models were developed using four machine learning algorithms: Random Forest (RF), extreme gradient boosting (XGBoost), Logistic Regression (LR), and Naïve Bayes (NB). This selection encompassed both traditional (LR, NB) and advanced ensemble methods (RF, XGBoost) to capture linear, probabilistic, and complex nonlinear relationships, enabling comprehensive comparison across modeling paradigms. Hyperparameters were optimized via grid search with stratified 5-fold cross-validation using ROC-AUC as the selection metric (Python 3.13, scikit-learn 1.3.0, XGBoost 1.7.0, random_state=42). The optimal configurations were as follows: RF (n_estimators=50, max_depth=None, min_samples_split=2, min_samples_leaf=4); XGBoost (objective“binary: logisti”, colsample_bytree=0.8, learning_rate=0.2, max_depth=3, n_estimators=50, subsample=0.9); LR (penalty“l”, C=10, solver“sag”, max_iter=1000); and NB (var_smoothing=1e-5). Model performance was internally validated using the testing set. Discrimination was evaluated using the area under the receiver operating characteristic curve (AUC), accuracy, precision, recall, and F1 score; Calibration was measured with the Brier score and clinical utility was examined through decision curve analysis (DCA).

Model Explanation

To improve the interpretability of the predictive model, this study utilized the SHAP method to interpret and visualize the optimal model. The SHAP values for each feature variable were calculated. Subsequently, a feature importance summary plot and SHAP beeswarm plots were created to quantitatively and intuitively illustrate the contribution magnitude and directional influence of each feature on the model’s predictions.

Result

Patient Characteristics

The incidence of DPN among the included subjects was 42.9% (623/1450), The prevalence rates in the training set and test set were 42.95% (436/1015) and 42.98% (187/435), respectively. No statistically significant differences were observed between the training and test cohorts for any variables, as shown in Table 1.

Table 1 Characteristics Between Training and Test Sets of Elderly Type 2 Diabetes Patients

Characteristics	Training Set (n=1015)	Test Set (n=435)	Statistic	P
Age (years)	68.00 (66.00,71.50)	68.00 (66.00,72.00)	0.023[b]	0.479
FT3 (pmol/L)	4.11 (3.60,4.61)	4.17 (3.72,4.67)	0.053[b]	0.11
Urine Creatinine (mg/dL)	100.00 (50.00,100.00)	100.00 (50.00,100.00)	0.051[b]	0.093
Urine Microalbumin (mg/L)	10.60 (10.00,30.00)	10.90 (10.00,33.60)	0.044[b]	0.162
LDL-C (mmol/L)	2.83 (2.07,3.51)	2.78 (2.17,3.65)	0.039[b]	0.244
Charlson Comorbidity Index	2.00 (1.00,2.00)	2.00 (1.00,2.00)	0.025[b]	0.427
HDL-C (mmol/L)	1.04 (0.88,1.25)	1.04 (0.87,1.26)	0.020[b]	0.544
Hip Circumference (cm)	96.00 (92.00,101.00)	96.00 (91.00,101.00)	0.019[b]	0.571
Abdominal Fat Area (cm^2)	80.70 (56.80,106.85)	80.60 (54.05,107.90)	0.016[b]	0.625
Disease Duration (years)	11.00 (5.00,18.00)	11.00 (5.00,18.00)	0.016[b]	0.636
Urine Albumin (mg/L)	20.00 (10.00,40.00)	20.00 (12.37,60.00)	0.014[b]	0.659
Waist Circumference (cm)	92.00 (86.00,98.00)	91.00 (85.00,98.00)	0.011[b]	0.735
Subcutaneous Fat Area (cm^2)	180.00 (142.05,224.60)	180.10 (139.00,225.25)	0.010[b]	0.765
C-peptide (ng/mL)	4.69 (2.56,7.02)	4.49 (2.63,7.35)	0.009[b]	0.777
HbA1c (%)	8.40 (7.20,10.10)	8.40 (7.20,10.20)	0.009[b]	0.774

(*Continued*)

Table 1 (Continued).

Characteristics	Training Set (n=1015)	Test Set (n=435)	Statistic	P
Hour Postprandial Insulin (μIU/mL)	28.29 (16.61,46.50)	27.01 (16.35,47.63)	0.008[b]	0.799
Hemoglobin (g/dL)	137.00 (126.00,149.00)	137.00 (125.00,149.00)	0.005[b]	0.885
BMI (kg/m^2)	24.80 (22.65,27.00)	24.60 (22.70,27.00)	0.003[b]	0.919
TC (mmol/L)	4.64 (3.88,5.44)	4.64 (3.91,5.44)	0.003[b]	0.939
TG (mmol/L)	1.43 (1.03,2.12)	1.49 (1.02,2.01)	0.002[b]	0.941
White Blood Cell (×109/L)	6.33 (5.21,7.47)	6.37 (5.18,7.41)	0.001[b]	0.984
Gender, n (%)			0.335[a]	0.563
Female	572 (56.40)	253 (58.20)		
Male	443 (43.60)	182 (41.80)		
Family History			1.541[a]	0.214
No	457 (45.00)	212 (48.70)		
Yes	558 (55.00)	223 (51.30)		
Nap Taking, n (%)			1.254[a]	0.263
No	688 (67.80)	281 (64.60)		
Yes	327 (32.20)	154 (35.40)		
PAD, n (%)			0.910[a]	0.340
No	893 (88.00)	391 (89.90)		
Yes	122 (12.00)	44 (10.10)		
Antihypertensive Medication, n (%)			0.0133[a]	0.908
No	481 (47.40)	204 (46.90)		
Yes	534 (52.60)	231 (53.10)		
Hypoglycemic Medication, n (%)			0.513[a]	0.474
No	120 (11.80)	58 (13.30)		
Yes	895 (88.20)	377 (86.70)		
Alcohol Consumption, n (%)			0.410[a]	0.522
No	601 (59.20)	249 (57.20)		
Yes	414 (40.80)	186 (42.80)		
Sedentary Behavior, n (%)			0.247[a]	0.619
No	439 (43.30)	195 (44.80)		
Yes	576 (56.70)	240 (55.20)		
SSB Intake, n (%)			0.022[a]	0.882
No	780 (76.80)	332 (76.30)		
Yes	235 (23.20)	103 (23.70)		
Hypertension History, n (%)			0.308[a]	0.579
No	435 (42.90)	194 (44.60)		
Yes	580 (57.10)	241 (55.40)		
Smoking, n (%)			0.291[a]	0.589
No	619 (61.00)	258 (59.30)		
Yes	396 (39.00)	177 (40.70)		
Annual Income, n (%)			0.963[a]	0.618
≤¥30,000	500 (49.30)	204 (46.90)		
>¥30,000	515 (50.70)	231 (53.10)		
Sleep Status, n (%)			0.399[a]	0.528
Good	641 (63.20)	283 (65.10)		
Poor	374 (36.80)	152 (34.90)		
Education Level, n (%)			0.152[a]	0.696
≤High School	538 (53.00)	225 (51.72)		
>High School	477 (47.00)	210 (48.28)		

(*Continued*)

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Table 1 (Continued).

Characteristics	Training Set (n=1015)	Test Set (n=435)	Statistic	P
Fish Intake, n (%)			1.966[a]	0.374
≤200g	482 (47.49)	210 (48.28)		
>200g	533 (52.51)	225 (51.72)		
Fruit & Vegetable Intake, n (%)			0.353[a]	0.553
≤500g	380 (37.44)	155 (35.63)		
>500g	635 (62.56)	280 (64.37)		
Abdominal Diagnosis, n (%)			0.250[b]	0.882
Visceral Obesity	320 (31.52)	133 (30.57)		
Normal	388 (38.23)	165 (37.93)		
Subcutaneous Obesity	307 (30.25)	137 (31.50)		
Peripheral Vascular Examination, n%			3.066[b]	0.216
Normal	160 (15.76)	56 (12.87)		
Intimal Roughness	142 (13.99)	72 (16.55)		
Plaque Formation	713 (70.25)	307 (70.58)		
Hypoglycemic Regimen, n (%)			0.152[b]	0.927
None	60 (5.91)	28 (6.44)		
Oral Medication	721 (71.04)	308 (70.80)		
Insulin & Medication	234 (23.05)	99 (22.76)		

Notes: [a]Chi-square test statistic (χ^2 value); [b]Mann–Whitney *U*-test statistic (Z value).

Feature Selection

The training set was categorized into a DPN group (n = 436) and a non-DPN group (n = 579). Univariable analysis identified 19 variables with statistically significant differences (P<0.05), as shown in Table 2. These variables were subsequently incorporated into a multivariable logistic regression analysis, which identified 9 independent predictive feature: CCI, diabetes duration, HbA1c, PAD, history of hypertension, smoking, sedentary behavior, sugar-sweetened beverage intake, and sleep status. The detailed results are shown in Table 3.

Table 2 Univariable Factors Analysis of DPN Selection Variables (Training Set, n=1015)

Variable	DPN (n=436)	Non-DPN (n=579)	Statistic	P
FT3 (pmol/L)	4.03 (3.56, 4.53)	4.20 (3.66, 4.67)	−0.108[b]	0.003
CCI	2.00 (2.00, 3.00)	1.00 (1.00, 2.00)	0.452[b]	<0.001
Disease Duration (years)	16.00 (12.00, 20.00)	5.00 (4.00, 14.00)	0.546[b]	<0.001
HB (g/dL)	136.00 (125.00, 147.00)	139.00 (127.00, 149.50)	−0.081[b]	0.028
Urine Creatinine (mg/dL)	50.00 (50.00, 100.00)	100.00 (50.00, 100.00)	−0.066[b]	0.049
Urine Albumin (mg/L)	20.00 (15.00, 60.00)	20.00 (10.00, 30.00)	0.092[b]	0.011
C-peptide (ng/mL)	3.98 (2.22, 6.23)	5.10 (2.87, 7.63)	0.168[b]	<0.001
HbA1c (%)	9.10 (7.88, 11.20)	7.80 (6.90, 9.30)	0.396[b]	<0.001
PAD, n (%)			144.245[a]	<0.001
No	322 (73.85)	571 (98.62)		
Yes	114 (26.15)	8 (1.38)		
Hypoglycemic Medication, n (%)			5.142[a]	0.023
No	40 (9.17)	80 (13.82)		
Yes	396 (90.83)	499 (86.18)		
Alcohol Consumption, n (%)			4.175[a]	0.041
No	274 (62.84)	327 (56.48)		
Yes	162 (37.16)	252 (43.52)		

(*Continued*)

Table 2 (Continued).

Variable	DPN (n=436)	Non-DPN (n=579)	Statistic	P
Smoking, n (%)			4.271[a]	0.039
No	250 (57.34)	369 (63.73)		
Yes	186 (42.66)	210 (36.27)		
Hypertension History, n (%)			7.843[a]	0.005
No	165 (37.84)	270 (46.63)		
Yes	271 (62.16)	309 (53.37)		
Sedentary Behavior, n (%)			50.595[a]	<0.001
No	133 (30.50)	306 (52.85)		
Yes	303 (69.50)	273 (47.15)		
Antihypertensive Medication, n (%)			5.589[a]	0.018
No	188 (43.12)	293 (50.60)		
Yes	248 (56.88)	286 (49.40)		
SSB Intake, n (%)			92.718[a]	<0.001
No	271 (62.16)	509 (87.91)		
Yes	165 (37.84)	70 (12.09)		
Sleep Status, n (%)			145.346[a]	<0.001
Good	253 (58.03)	458 (79.10)		
Poor	183 (41.97)	121 (20.90)		
Education Level, n (%)			4.185[a]	0.041
≤High School	215 (49.31)	323 (55.79)		
>High School	221 (50.69)	256 (44.21)		
Hypoglycemic Regimen, n (%)			58.092[b]	<0.001
None	24 (5.51)	36 (6.22)		
Insulin & Medication	151 (34.63)	83 (14.33)		
Oral Medication Only	261 (59.86)	460 (79.45)		

Notes: [a]Chi-square test statistic (χ^2 value); [b]Mann–Whitney *U*-test statistic (Z value).

Table 3 Multivariable Factors Analysis of DPN Selection Variables (Training Set, n=1015)

Factor	β-Coefficient	Standard Error	Z-value	OR	95% CI	*P*
Disease Duration (years)	0.120	0.014	8.596	1.127	1.098–1.158	<0.001
HbA1c (%)	0.370	0.052	7.096	1.448	1.307–1.603	<0.001
Poor Sleep Status	1.834	0.205	8.928	6.258	4.184–9.360	<0.001
CCI	0.693	0.111	6.259	2.000	1.610–2.485	<0.001
SSB Intake	1.702	0.242	7.041	5.487	3.416–8.813	<0.001
PAD	2.294	0.462	4.965	9.911	4.008–24.508	<0.001
Sedentary Behavior	0.991	0.203	4.885	2.693	1.810–4.007	<0.001
Smoking	0.537	0.230	2.334	1.711	1.090–2.687	0.020
Hypertension	0.991	0.439	2.727	3.306	1.310~7.810	0.006

Model Performance

Using the occurrence of DPN as the dependent variable and the nine previously screened variables as independent variables, we constructed four prediction models based on RF, XGBoost, LR, and NB. The performance evaluation demonstrated that the XGBoost model achieved the highest scores across all metrics except Accuracy, as shown in Table 4. The ROC analysis on the training set (Figure 1A) showed that all models achieved high AUC values, indicating excellent discriminative ability during training. In the test set (Figure 1B), the XGBoost model achieved the highest AUC (0.951) among all models. To assess calibration performance, the Hosmer-Lemeshow goodness-of-fit test was conducted, the XGBoost model demonstrated superior performance in the test set, yielding a χ^2value of 4.935 with a P-value of

Table 4 Performance Evaluation of the Four Prediction Models

Model	Dataset	AUC	Accuracy	Precision	Recall	F1-Score	Brier
LR	Training	0.917	0.834	0.814	0.794	0.804	0.114
	Test	0.917	0.848	0.854	0.781	0.816	0.114
RF	Training	0.986	0.933	0.926	0.917	0.922	0.056
	Test	0.940	0.869	0.865	0.824	0.844	0.097
XGBoost	Training	0.973	0.914	0.905	0.895	0.900	0.065
	Test	0.951	0.878	0.876	0.834	0.855	0.087
NB	Training	0.901	0.816	0.881	0.661	0.755	0.141
	Test	0.905	0.816	0.879	0.663	0.756	0.142

0.668, indicating no significant deviation between the predicted and observed outcomes. Furthermore, the calibration curves closely aligned with the ideal reference line (Figure 1C and D), suggesting strong agreement between predicted probabilities and actual event probabilities. DCA revealed that in the training set, the RF model outperformed all other models across a broad threshold probability range of 0–0.8 (Figure 1E). However, in the test set, the XGBoost model provided the highest net benefit across nearly the entire threshold range (0–0.9, Figure 1F). Based on this comprehensive assessment of discrimination, calibration, and clinical applicability, the XGBoost model was identified as the optimal predictive model.

Model Explanation

We utilized the SHAP method to interpret the XGBoost model by calculating the contribution of each variable to the predictions. Figure 2 displays the average SHAP values for each feature, with the relative contributions of the feature variables ranked in descending order as follows: diabetes duration, HbA1c, sleep status, CCI, sugar-sweetened beverage intake, PDA, sedentary behavior, smoking, and hypertension, underscoring their pivotal role in predicting DPN. SHAP swarm Plot visualizes feature importance, with each point corresponds to a sample, and a color gradient from blue (low values) to red (high values) reflects the magnitude of the feature value. The vertical axis displays the ranked features, showing the correlation and distribution of feature values with their corresponding SHAP values.

Discussion

The findings of this study demonstrate that disease duration (OR=1.127, P< 0.001) and HbA1c level (OR=1.448, P<0.001) are significant risk factors for DPN in elderly patients with T2DM. Previous studies have also showed that patients with T2DM for more than 10 years have a markedly increased risk of neuropathy, with each additional year of disease duration raising the risk of DPN by approximately 7%.[27–29] This underlying pathological mechanism may be linked to cumulative microvascular and neural damage, which is mediated by the "metabolic memory effect". In terms of glycemic control, HbA1c level showed a significant positive correlation with DPN risk. Supporting the findings of Wu and Darivemula.[9,30] It was further quantified that individuals with HbA1c >7% had a 4.81-fold increased risk of DPN. This mechanism is primarily attributed to persistent hyperglycemia, which promotes the excessive formation of advanced glycation end products(AGEs), leading to endometrial ischemia and disruption of the blood-nerve barrier.[31] Notably, unlike previous studies, this research specifically focuses on elderly T2DM patients. This population may exhibit greater susceptibility to long-term hyperglycemia and the metabolic memory effect due to age-related declines in neural repair capacity and vascular function. Therefore, the following targeted strategies are recommended for clinical practice: first, establish disease duration-stratified management pathway. For elderly patients with T2DM and a disease duration ≥ 10years, standardized examinations for peripheral neurological signs should be conducted semi-annually, and personal health records should be established to systematically monitor disease progression. In contrast, for those with a duration <10 years, annual screening should be prioritized, combined with preventive education, specifically guiding them in recognizing early symptoms such as limb numbness and pain. Furthermore, individualized glycemic management must be implemented. HbA1c targets should be personalized, considering the patient's overall health status. For elderly

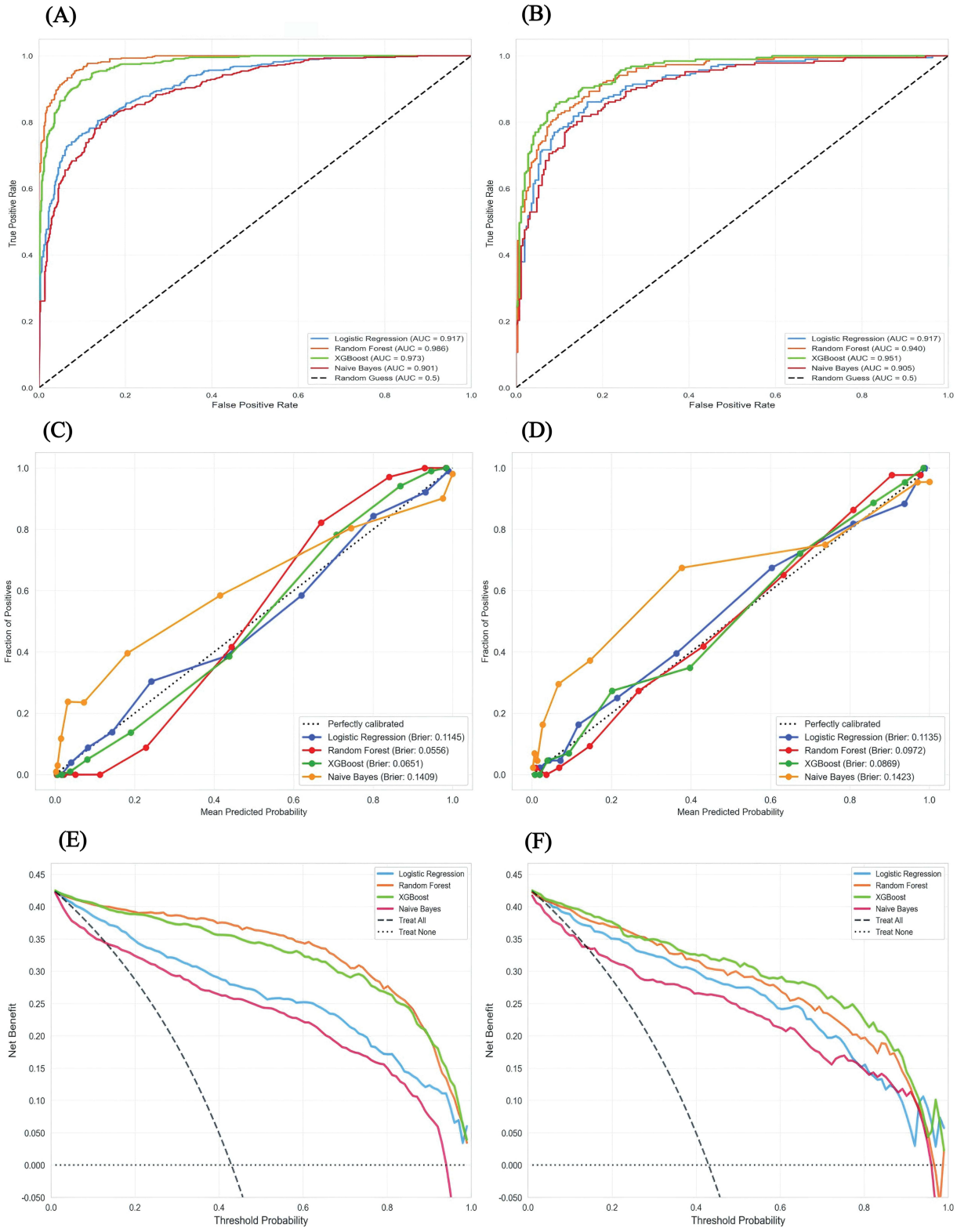

Figure 1 Performance and comparison of four predictive models.(**A**) ROC curves for the training set. (**B**) ROC curves for the test set.(**C**) Calibration curves for the training set. (**D**) Calibration curves for the test set.(**E**) Decision curve analysis (DCA) for the training set. (**F**) Decision curve analysis (DCA) for the test set.

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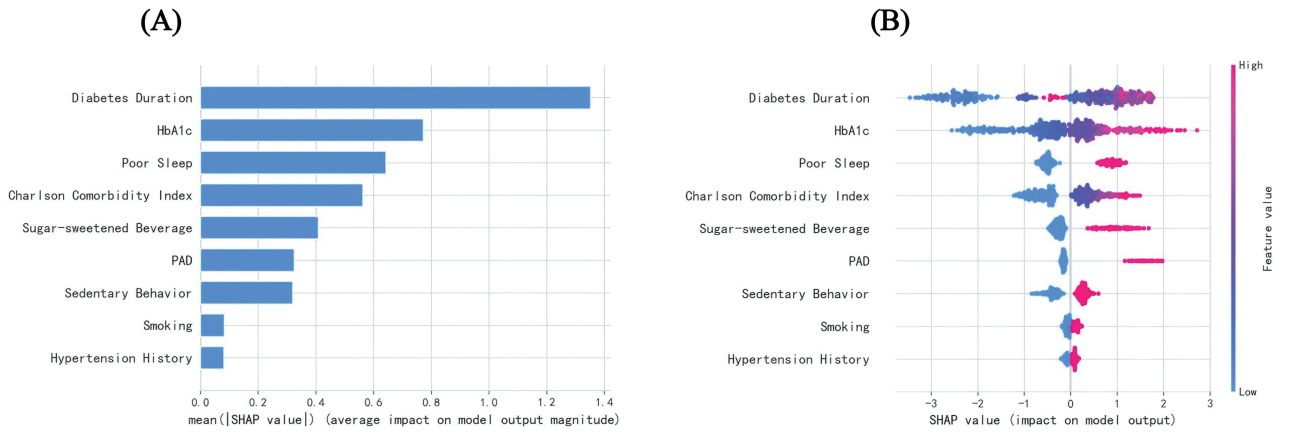

Figure 2 SHAP analysis for feature interpretability. (**A**) Feature importance ranking for the XGBoost model. (**B**) SHAP Beeswarm Plot of features for the XGBoost model.

patients with multiple chronic conditions or frailty, these targets may be appropriately relaxed to 8.0–8.5% to balance potential risks and benefits.[32] Simultaneously, a multidimensional support network should be developed, incorporating family members, peers, and digital tools. By engaging family in daily management, organizing peer support groups for diabetes,[33] and utilizing health platforms with data-sharing capabilities,[34] continuous glucose monitoring and timely feedback can be achieved. These measures can effectively delay the onset and progression of DPN and improve the quality of life for elderly diabetic patients.

The findings of this study also indicate that the CCI (OR = 2.000, P < 0.001), PAD (OR = 9.911, P < 0.001), and history of hypertension (OR = 3.306, P < 0.001) are independent risk factors for DPN in this population. A higher CCI score signifies multiple chronic conditions, which may interact with diabetic metabolic dysregulation through chronic inflammatory pathways, thereby accelerating nerve damage progression, consistent with the findings of Luo.[11] PAD, as a manifestation of systemic atherosclerosis, indicates significant macrovascular pathology in the lower limbs, directly leading to hypoperfusion in the neural microcirculation and placing nerve fibers in a persistent ischemic and hypoxic environment.[35] Hypertension impairs vascular endothelial function and exacerbates microcirculatory disorders, disrupting blood-nerve barrier integrity in conjunction with hyperglycemia.[36] Clinical evidence demonstrates a significant delay in DPN onset and improvement in nerve conduction function among patients using Angiotensin-Converting Enzyme Inhibitors (ACEIs),[37] validating the critical role of blood pressure management in neuroprotection. Therefore, a comprehensive management strategy is recommended for elderly T2DM patients with these comorbidities: establish a comorbidity assessment system incorporating the CCI as a mandatory component of regular evaluations and initiate multidisciplinary collaborative management for patients with multiple chronic conditions; Enhance PAD screening by regularly assessing vascular status using objective measures such as the ankle-brachial index. For patients with hypertension, it is crucial to prioritize antihypertensive agents with potential neuroprotective properties, such as ACEIs, while emphasizing that blood pressure control is as critical as glycemic management. Multifactorial integrated interventions can effectively reduce the DPN risk in elderly patients with T2DM.

The results further demonstrate that poor sleep quality (OR = 6.258, P < 0.001), sugar-sweetened beverage intake (OR = 5.487, P < 0.001), sedentary behavior (OR = 2.693, P < 0.001), and smoking (OR = 1.711, P < 0.001) are independent, modifiable behavioral risk factors for DPN. These factors collectively promote DPN onset and progression through multiple interacting pathophysiological pathways. A bidirectional vicious cycle exists between sleep disorders and DPN: sleep disorders activate the hypothalamic-pituitary-adrenal axis and sympathetic nervous system, triggering systemic inflammation and oxidative stress responses, exacerbating insulin resistance and metabolic disturbances, thereby promoting neural damage.[38,39] Conversely, neuropathic pain and paresthesia caused by DPN disrupt sleep architecture and quality.[40] Frequent consumption of sugar-sweetened beverages not only impairs pancreatic β-cell function through glucotoxicity but also induces massive reactive oxygen species production, leading to oxidative stress damage. These mechanisms collectively compromise the integrity of the blood-nerve barrier and impair neuronal structure and

function.[41] A clear dose-response relationship exists between sedentary behavior and DPN risk. Research by Loprinzi et al indicated that both T2DM and DPN are independently associated with lower levels of physical activity and higher sedentary time.[42] This association likely arises because prolonged sitting impedes venous return in the lower limbs, suppresses the muscle pump function, and causes inadequate perfusion and hypoxia in neural tissues, ultimately promoting nerve fiber degeneration.[43] Conversely, regular exercise not only improves local neural blood flow and promotes the release of neurotrophic factors and nerve regeneration, but also exerts protective effects through systemic metabolic regulation.[44,45] Furthermore, studies have identified a significant positive correlation between sleep deprivation and sedentary behavior, with both factors producing synergistic detrimental effects through weight gain and insulin resistance.[46] Smoking increases DPN risk through multiple mechanisms, including inducing insulin resistance, promoting atherosclerosis, exacerbating systemic inflammatory responses, and impairing vascular endothelial function.[47,48] Based on these findings, comprehensive interventions targeting these modifiable behavioral factors are recommended. Such as establishing regular sleep schedules, providing sleep education, and implementing cognitive behavioral therapy to improve sleep quality; developing individualized sedentary behavior intervention plans addressing psychological and behavioral aspects,[49] incorporating daily moderate aerobic and resistance training; delivering nutritional guidance that explicitly restricts sugar-sweetened beverage consumption; and providing systematic smoking cessation support and follow-up. Establishing a prevention and control system centered on behavior management for DPN will effectively delay disease progression and improve patients' quality of life.

This study developed a risk prediction model for DPN among older adults with T2DM. Systematic evaluations indicated that the XGBoost model achieved the best overall performance. In the study by Sun et al, although ten-fold cross-validation was used to improve model stability, the AUC dropped substantially from 0.933 in internal validation to 0.811 in an independent test set, reflecting notable performance variation across datasets.[14] Our model maintained high and comparable performance in both the training and test sets (AUCs of 0.973 and 0.951, respectively), with decision curve analysis demonstrating stable net benefits across a wide threshold range (0–0.9). Beyond predictive performance, the clinical feasibility of a model depends on its feature selection. Liu et al incorporated inflammatory biomarkers such as C-reactive protein and total bile acid to improve predictive accuracy; however, these laboratory-dependent features are more feasible in resource-intensive inpatient settings, thereby limiting their generalizability to outpatient elderly populations.[15] While Jiang et al employed traditional Chinese medicine symptom features that rely heavily on patient-reported information and physician interpretation, which may restrict standardization and cross-institutional applicability.[13] In contrast, our model leverages the MMC platform's standardized electronic follow-up system, integrating objective clinical indicators, such as HbA1c, as well as lifestyle factors derived from structured questionnaires, including sleep duration, exercise intensity, and sugar-sweetened beverage intake, ensuring both accessibility and reproducibility. Overall, the proposed model combines high predictive performance with standardized, easily obtainable features, enhancing its applicability and scalability for managing chronic disease in elderly T2DM patients.

To enhance interpretability, SHAP analysis was employed to visualize the contribution of each variable. The SHAP summary and dependence plots indicated that diabetes duration and HbA1c were the strongest contributors to a higher predicted risk of DPN, aligning with the well-established roles of long-term hyperglycemia, metabolic memory, and microvascular injury in neuropathy progression. Lifestyle behaviors, including poor sleep quality, sedentary time, and sugar-sweetened beverage intake, also demonstrated substantial positive SHAP values, indicating their meaningful influence on individual risk profiles. In addition, clinical comorbidities such as PAD, higher CCI scores, hypertension, and smoking showed pronounced SHAP contributions, suggesting cumulative risk effects in elderly patients. Consistent with the approach of Sun et al, who used SHAP to enhance transparency,[14] this study further identifies potential targets for lifestyle intervention, providing actionable guidance for the personalized health management of elderly patients and supporting its potential integration of this predictive model into structured management platforms such as the MMC system to facilitate early screening and targeted intervention for DPN in elderly T2DM patients.

Limitations

In this study, several limitations should be acknowledged. First, this study used a retrospective design, which may introduce information bias. Second, the data were derived from a single center, limiting representativeness and

potentially restricting the model's applicability to other populations. Third, although the model achieved strong performance in internal validation, external validation using independent multi-center datasets was not conducted, which limits generalizability. Future studies should therefore include prospective, multi-center cohorts with external validation to further refine the model and enhance its clinical utility.

Conclusion

This study developed a risk prediction model for DPN in elderly patients with T2DM using four machine learning algorithms. Through comprehensive evaluation and comparison, the XGBoost model exhibited optimal performance in terms of discrimination, calibration, and clinical utility, indicating its potential value as an early screening tool in clinical practice. The model enables rapid identification of high-risk individuals based on easily obtainable clinical and lifestyle indicators, which may assist clinicians in implementing timely risk stratification and targeted interventions. Through variable importance analysis, we identified diabetes duration, HbA1c, poor sleep, CCI, sugar-sweetened beverage intake, PAD, sedentary behavior, smoking and hypertension as key predictors. These findings provide a valuable reference for identifying elderly T2DM patients at high risk of developing DPN. However, the model was developed using retrospective, single-center data and without external validation in independent cohorts, which may limit its generalizability. Future research should focus on multi-center, large-sample prospective studies with external validation to continuously optimize model performance and enhance its clinical applicability and generalizability.

Data Sharing Statement

The data used to support the findings of this study are available from the corresponding author upon request.

Ethics Approval and Consent to Participate

This study followed the principles of the Declaration of Helsinki and was approved by the ethics committee of Gongli hospital of Shanghai Pudong New Area (Approval No: GLYYls2024-066). The requirement for informed consent was waived by the same ethics committee due to the retrospective nature of the study.

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Author Contributions

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 in this work.

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