

A Nomogram for Predicting 5-Year Risk of New-Onset Type 2 Diabetes in Patients with COPD: A Two-Center Retrospective Cohort Study

Jingjing Pan^{1,*}, Feiju Chen^{1,*}, Weifeng Liao¹, Weilong Ye¹, Bainian Chen¹, Tong Lu¹, Kunning Li¹, Fang Liu¹, Xuyu Deng¹, Ting Sun¹, Riken Chen¹, Weimin Yao^{1,2}

¹Department of Respiratory and Critical Care Medicine, The Second Affiliated Hospital of Guangdong Medical University, Zhanjiang, Guangdong, 524003, People's Republic of China; ²Institute of Respiratory Diseases, Affiliated Hospital of Guangdong Medical University, Zhanjiang, Guangdong, 524003, People's Republic of China

*These authors contributed equally to this work

Correspondence: Riken Chen; Weimin Yao, Department of Respiratory and Critical Care Medicine, The Second Affiliated Hospital of Guangdong Medical University, Zhanjiang, Guangdong, 524003, People's Republic of China, Tel +8613560244631; +8613822521722, Email chenriken@126.com; 490296443@qq.com

Purpose: Type 2 diabetes mellitus (T2DM) often coexists with chronic obstructive pulmonary disease (COPD) and is accompanied by adverse outcomes, including high mortality. We developed and externally validated a nomogram to predict the 5-year new-onset T2DM risk in COPD patients without prior diabetes.

Patients and Methods: Patients hospitalized for COPD between May 2018 and December 2019 were enrolled and followed until December 2024. The development cohort was randomly divided into training and internal validation sets at a 7:3 ratio. In the training set, predictors were selected via least absolute shrinkage and selection operator (LASSO) regression and used to construct a nomogram. Model discrimination was evaluated by the receiver operating characteristic (ROC) curve with the area under the curve (AUC). Calibration curves and decision curve analysis (DCA) were used to assess calibration and clinical utility.

Results: A total of 998 patients in our development cohort, 153 (15.3%) developed new-onset T2DM during follow-up. The final nomogram contained four predictors: Triglyceride–glucose index (TyG), hypertension (HTN), cardiovascular disease (CVD), and high-density lipoprotein (HDL). The AUCs in the training and internal validation sets were 0.749 and 0.758. External validation in an independent cohort of 1,018 patients, including 132 incident T2DM cases, produced an AUC of 0.798. DCA plots showed net clinical benefit across clinically relevant thresholds.

Conclusion: This nomogram demonstrated good discrimination and calibration, and may facilitate risk stratification for T2DM among COPD patients.

Keywords: chronic obstructive pulmonary disease, diabetes mellitus, prediction model, nomogram

Introduction

Chronic obstructive pulmonary disease (COPD) is a chronic inflammatory airway condition. Its key feature is persistent airflow limitation.¹ COPD is mainly related to prolonged exposure to tobacco smoke and other environmental pollutants, accompanied by systemic inflammation and immune dysregulation.^{2–4} Globally, COPD imposes substantial mortality and morbidity and continues to rise.^{5,6} In China, the prevalence of COPD has increased over the past decades, resulting in a significant healthcare burden.⁷

Extrapulmonary comorbidities are common in COPD and are associated with worse outcomes. Typical examples include cardiovascular disease (CVD), metabolic syndrome, anxiety and depression.^{8,9} More than half of COPD patients have four or more comorbidities.¹⁰ These comorbidities may accelerate disease progression through systemic

inflammation and metabolic dysregulation.^{11,12} Notably, metabolic syndrome is common and correlates with increased all-cause mortality.¹³ As a metabolic comorbidity closely related to metabolic syndrome, T2DM is common in COPD. In COPD, T2DM is linked to more frequent exacerbations, slower recovery of lung function, and higher mortality.^{14–16} Epidemiological data consistently show that T2DM prevalence in COPD exceeds that observed in the general population.^{17,18}

Prior studies have analyzed risk factors for T2DM in patients with COPD. In a large cohort study involving over 220,000 COPD patients, frequent exacerbations and inhaled corticosteroids (ICS) use were associated with subsequent T2DM in COPD patients.¹⁹ Another cohort study in Taiwan indicated that hypertension and higher triglyceride levels were independent risk factors.²⁰ However, it remains unclear whether COPD patients with normal baseline blood glucose levels will develop T2DM within the next 3 to 5 years. Currently, no predictive model exists to forecast the risk of T2DM occurrence within 5 years in clinically diagnosed COPD patients. Therefore, developing a simple clinical prediction tool to assess the likelihood of COPD patients developing T2DM within five years would be of significant importance.

Materials and Methods

Study Population

This was a two-center retrospective cohort study. We consecutively included COPD patients hospitalized between May 2018 and December 2019 at either the Affiliated Hospital or the Second Affiliated Hospital of Guangdong Medical University as the baseline study population. To avoid duplicate records, we retained only the first admission for patients with multiple admissions. COPD was ascertained from medical records based on physician-documented discharge diagnoses and independently verified by two investigators through chart review in the EMR. Spirometry reports were available only for a subset of patients; when available, airflow limitation ($FEV_1/FVC < 0.70$) was used to support the diagnosis in accordance with GOLD recommendations.²¹

Eligibility criteria: Adults (≥ 18 years) hospitalized with a physician-diagnosed COPD documented in the medical record were eligible if baseline data were available and follow-up information could be obtained. Patients were excluded if they had other major respiratory diseases (including bronchiectasis, active pulmonary tuberculosis, or interstitial lung disease), a prior diagnosis of diabetes or impaired glucose tolerance at baseline, missing key laboratory variables, unavailable outcome follow-up, or coexisting malignancy or autoimmune disease.

Outcome definition: Incident T2DM was identified according to the American Diabetes Association (ADA) criteria.²² Diagnosis required meeting at least one of the criteria below:

1. classic hyperglycemic symptoms (polyuria, polydipsia, polyphagia, and unexplained weight loss) plus a random plasma glucose ≥ 11.1 mmol/L.
2. fasting plasma glucose ≥ 7.0 mmol/L or HbA1c $\geq 6.5\%$.

In asymptomatic individuals, the results were confirmed on a separate day.

Follow-Up and Outcome Determination

Patients were followed from their initial hospitalization to the earliest of: (1) incident T2DM; (2) 5 years after the first hospitalization. Follow-up strategy was performed using passive monitoring through the hospital electronic medical record (EMR) system with active telephone follow-up.

1. Passive follow-up: Outpatient and inpatient medical records were reviewed via the EMR system to determine diabetes status. After completion of the follow-up period, we performed a one-time retrospective, standardized EMR search for each participant to retrieve all available outpatient and inpatient encounter records. Incident

T2DM was defined as the first recorded diagnosis of T2DM or documentation of laboratory values meeting the diagnostic criteria during follow-up. In addition to searching recorded diagnoses, we systematically screened all available glycemic laboratory results recorded in the EMR during follow-up to identify cases meeting diagnostic criteria even if no diagnosis code was entered.

2. Active follow-up: For patients without adequate EMR follow-up, trained researchers conducted telephone interviews between January 2024 and June 2025 to ascertain whether a physician diagnosis of T2DM had been made during the prespecified follow-up period and whether continuous glucose-lowering therapy had been initiated. During telephone interviews, a self-reported physician diagnosis of T2DM was accepted when accompanied by ongoing glucose-lowering medication use, and participants were asked to report the medication name and start date when possible.

Without adequate EMR follow-up was defined as having no subsequent healthcare encounters such as outpatient, emergency, or inpatient visits, and no glycemic laboratory records documented in our EMR system after discharge from the index hospitalization until the end of the follow-up period, suggesting follow-up outside our network.

Patients without incident T2DM by the last date and with valid follow-up information were classified as non-events.

Data Collection

Variables were selected according to clinical relevance and routinely collected clinical data. Data were extracted from the EMR at the first hospitalization and included the following categories:

1. General characteristics: sex, age, blood pressure, duration of COPD, smoking history, alcohol drinking history;
2. Laboratory parameters: white blood cell count (WBC), neutrophil count (N), lymphocyte count (LYM), monocyte count (MON), hemoglobin (HB), hematocrit (HCT), platelets (PLT), procalcitonin (PCT), alanine aminotransferase (ALT), serum potassium (K) and sodium (Na), uric acid (UA), high-density lipoprotein (HDL), low-density lipoprotein (LDL), estimated glomerular filtration rate (eGFR), fibrinogen (FIB), activated partial thromboplastin time (APTT), triglyceride-glucose index (TyG), prognostic nutritional index (PNI). Fasting plasma glucose (FPG), fasting triglycerides (TG), and serum albumin (ALB) were extracted to derive TyG and PNI and were not entered as separate predictors to avoid multicollinearity. The TyG index was calculated as $\ln [TG \text{ (mg/dL)} \times FPG \text{ (mg/dL)} / 2]$, with TG and FPG values recorded in mmol/L converted to mg/dL before calculation ($TG \times 88.57$; $FPG \times 18.0$).²³ PNI was calculated as $\text{albumin (g/L)} + 5 \times \text{lymphocyte count (10}^9\text{/L)}$.²⁴
3. Comorbidities and medication history: hypertension (HTN), cardiovascular disease (CVD), hematologic disorders, malignancies, glucocorticoid exposure (route and duration), and use of anticoagulants, antiplatelet agents, and statins. Glucocorticoid exposure was assessed at the index hospitalization and categorized as none, inhaled (including inhaled corticosteroids and nebulized inhaled glucocorticoids), or systemic (oral or intravenous).

Data Pre-Processing

All data cleaning and modeling analyses were conducted in R 4.4.3. Categorical variables were coded as a factor, and continuous variables were retained as numeric. The CheckMissing was used to package to summarize missingness for each variable. Variables with > 20% missingness were removed, whereas missing values $\leq 20\%$ were imputed using multiple imputation by chained equations (MICE).^{25,26} The outcome variable were excluded from the imputation model. Based on follow-up outcomes, participants were classified into a new-onset T2DM group and a non-T2DM group. In the development cohort, we used the createDataPartition function in the caret package to randomly split the data in a 7:3 ratio. A fixed random seed was used to ensure reproducibility of the analyses.

Statistical Analysis and Model Development

Univariable and multivariable logistic regression analyses were conducted to evaluate independent factors associated with new-onset T2DM ($P < 0.05$). Separately, for nomogram development, all baseline variables in Table 1 were subjected to feature selection using LASSO logistic regression with the glmnet package. FPG, TG, and albumin were used to derive TyG

Table 1 Baseline Balance Test Between the Training Cohort and Internal Validation Cohort

Variables	Total (n = 998)	Validation (n = 298)	Train (n = 700)	P value
Sex				0.722
Female	262 (26.3%)	81 (27.2%)	181 (25.9%)	
Male	736 (73.7%)	217 (72.8%)	519 (74.1%)	
Smoking history				0.568
No	601 (60.2%)	184 (61.7%)	417 (59.6%)	
Yes	397 (39.8%)	114 (38.3%)	283 (40.4%)	
Alcohol drinking history				0.895
No	921 (92.3%)	274 (91.9%)	647 (92.4%)	
Yes	77 (7.7%)	24 (8.1%)	53 (7.6%)	
HTN				0.208
No	571 (57.2%)	180 (60.4%)	391 (55.9%)	
Yes	427 (42.8%)	118 (39.6%)	309 (44.1%)	
CVD				1.000
No	584 (58.5%)	174 (58.4%)	410 (58.6%)	
Yes	414 (41.5%)	124 (41.6%)	290 (41.4%)	
Antithromb Use				0.861
No	597 (59.8%)	180 (60.4%)	417 (59.6%)	
Yes	401 (40.2%)	118 (39.6%)	283 (40.4%)	
GC Route				0.133
Systemic	514 (51.5%)	154 (51.7%)	360 (51.4%)	
Inhaled	215 (21.5%)	74 (24.8%)	141 (20.1%)	
None	269 (27.0%)	70 (23.5%)	199 (28.4%)	
Statin use				0.152
No	700 (70.1%)	219 (73.5%)	481 (68.7%)	
Yes	298 (29.9%)	79 (26.5%)	219 (31.3%)	
Age	78.00 [69.00, 84.00]	78.00 [70.00, 84.75]	78.00 [69.00, 84.00]	0.736
LOS days	9.00 [7.00, 13.00]	9.00 [6.00, 13.00]	9.00 [7.00, 13.00]	0.883
COPD Duration	10.00 [5.00, 12.00]	10.00 [5.00, 15.00]	10.00 [5.00, 11.25]	0.111
SBP (mmHg)	137.00 [122.00, 154.00]	138.00 [122.00, 156.00]	137.00 [122.00, 154.00]	0.758
GC Days	6.00 [0.00, 10.00]	6.00 [1.00, 10.00]	6.00 [0.00, 10.00]	0.231
WBC ($\times 10^9/L$)	7.82 [6.21, 10.60]	7.63 [6.08, 10.19]	7.87 [6.23, 10.75]	0.425
N ($\times 10^9/L$)	5.63 [4.09, 8.28]	5.50 [4.25, 7.86]	5.69 [4.05, 8.42]	0.621
LYM ($\times 10^9/L$)	1.13 [0.76, 1.60]	1.11 [0.73, 1.51]	1.13 [0.76, 1.62]	0.623
MON ($\times 10^9/L$)	0.64 [0.44, 0.83]	0.63 [0.44, 0.83]	0.64 [0.43, 0.83]	0.866
HB (g/L)	125.95 [113.00, 138.70]	126.10 [112.55, 138.38]	125.45 [113.00, 138.80]	0.848
HCT (%)	38.30 [34.60, 42.20]	38.30 [34.82, 42.38]	38.30 [34.40, 42.20]	0.634
PLT ($\times 10^9/L$)	208.00 [166.02, 255.17]	203.00 [161.22, 251.00]	210.00 [168.68, 260.45]	0.236
PCT (ng/mL)	0.09 [0.02, 0.20]	0.09 [0.02, 0.20]	0.09 [0.02, 0.20]	0.868
ALT (U/L)	15.10 [10.60, 23.30]	14.80 [10.53, 22.58]	15.10 [10.60, 23.50]	0.706
K (mmol/L)	4.03 [3.72, 4.34]	4.05 [3.71, 4.36]	4.02 [3.72, 4.34]	0.783
Na (mmol/L)	140.10 [137.50, 142.30]	140.15 [137.55, 142.50]	140.10 [137.50, 142.10]	0.530
UA ($\mu\text{mol/L}$)	301.55 [227.62, 389.98]	309.40 [235.50, 396.60]	299.55 [223.28, 384.30]	0.314
HDL (mmol/L)	1.39 [1.12, 1.71]	1.40 [1.14, 1.75]	1.39 [1.10, 1.69]	0.324
LDL (mmol/L)	2.46 [1.86, 3.16]	2.55 [1.99, 3.12]	2.43 [1.86, 3.17]	0.311

(Continued)

Table 1 (Continued).

Variables	Total (n = 998)	Validation (n = 298)	Train (n = 700)	P value
eGFR (mL/min/1.73 m ²)	82.67 [66.14, 92.93]	82.65 [65.93, 91.78]	82.80 [66.27, 93.38]	0.408
APTT (s)	33.40 [28.80, 38.80]	33.25 [28.80, 38.77]	33.60 [28.78, 38.80]	0.439
FIB (g/L)	3.75 [2.94, 4.55]	3.76 [2.90, 4.48]	3.75 [2.96, 4.57]	0.655
TyG	8.16 [7.87, 8.51]	8.16 [7.86, 8.52]	8.16 [7.88, 8.50]	0.837
PNI	42.75 [39.00, 47.00]	42.90 [38.70, 47.11]	42.75 [39.04, 46.95]	0.615

Abbreviations: HTN, hypertension; CVD, cardiovascular disease; Antithromb Use, use of anticoagulants and/or antiplatelet agents; GC Route, route of glucocorticoid administration at the index hospitalization (none indicates no glucocorticoid use; inhaled includes inhaled corticosteroids and nebulized inhaled glucocorticoids); systemic indicates oral or intravenous glucocorticoids; Statin Use, statin use; LOS days, length of hospital stay; SBP, systolic blood pressure; GC Days, duration of glucocorticoid use; WBC, white blood cell count; N, neutrophil count; LYM, lymphocyte count; MON, monocyte count; HB, hemoglobin; HCT, hematocrit; PLT, platelet count; PCT, procalcitonin; ALT, alanine aminotransferase; K, serum potassium; Na, serum sodium; UA, uric acid; HDL, high-density lipoprotein; LDL, low-density lipoprotein; eGFR, estimated glomerular filtration rate; APTT, activated partial thromboplastin time; FIB, fibrinogen; TyG, triglyceride–glucose index; PNI, prognostic nutritional index. TyG = $\ln [TG (mg/dL) \times FPG (mg/dL) / 2]$; TG and FPG measured in mmol/L were converted to mg/dL before calculation ($TG \times 88.57$; $FPG \times 18.0$). PNI = albumin (g/L) + 5 × lymphocyte count ($10^9/L$).

and PNI and were therefore not entered separately to avoid multicollinearity. The tuning parameter λ was selected by 10-fold cross-validation, and variables with non-zero coefficients at $\lambda_{\min}$ were retained.²⁷ To reduce model complexity and enhance clinical applicability, the final nomogram was constructed using the four predictors with the largest absolute LASSO coefficients. These predictors were included in a multivariable logistic regression model (rms package, lrm) to build the nomogram.

Model Validation and Evaluation

Model performance was assessed for discrimination, calibration, and clinical utility. Discrimination was summarized by the AUC of the ROC curve. Calibration was assessed by comparing predicted probabilities and observed events using calibration plots, and internal calibration was further examined with 500 bootstrap resamples. Clinical benefit was explored using DCA across a range of threshold probabilities.

Because incident T2DM was relatively infrequent, using the conventional 0.5 probability threshold for classification may not be suitable. Therefore, we determined the optimal probability threshold in the internal validation cohort by maximizing the F1 score, and then applied it to the external validation cohort to keep thresholding consistent across datasets.

Model robustness was assessed using 10-fold cross-validation in the training set. An independent COPD cohort from the Second Affiliated Hospital of Guangdong Medical University was used for external validation. Subgroup analyses were conducted separately for sex, age (<65 years and ≥65 years), and hypertension status to evaluate subgroup consistency.

Statistical Methods

Statistical analyses were performed in R 4.4.3. The Shapiro–Wilk test was used to guide descriptive summaries. Continuous variables were expressed as mean ± standard deviation (SD) or median (interquartile range, IQR), and categorical variables as counts and percentages. Group comparisons were assessed using Student's *t* test or the Wilcoxon rank-sum test for continuous variables, and the χ^2 -test or Fisher's exact test for categorical variables. A two-sided *P* value <0.05 was considered statistically significant.

Results

Training Set Baseline Comparison

In the development cohort, 998 patients with COPD were included, and 153 developed incident T2DM. The median age was 78.0 years (IQR: 69.0–84.0). Men accounted for 736 participants (73.7%), and women for 262 (26.3%). The dataset was split 7:3 into a training (n=700) and an internal validation (n=298) set randomly. The two sets were well balanced in

baseline characteristics (Table 1). Within the training set, median age was higher in the incident T2DM group, and HTN, CVD were more common than in the non-T2DM group. The use of anticoagulants or antiplatelet agents and statins was also higher. Additionally, these patients had higher TyG index, PCT, and SBP levels, while HDL and APTT levels were lower (*all P* < 0.05) (Table 2).

Table 2 Baseline Characteristics of the Training Set

Variables	Total (n = 700)	No DM (n = 592)	DM (n = 108)	P value
Sex				0.274
Female	181 (25.9)	148 (25.0)	33 (30.6)	
Male	519 (74.1)	444 (75.0)	75 (69.4)	
Smoking history				0.375
No	417 (59.6)	348 (58.8)	69 (63.9)	
Yes	283 (40.4)	244 (41.2)	39 (36.1)	
Alcohol drinking history				0.601
No	647 (92.4)	549 (92.7)	98 (90.7)	
Yes	53 (7.6)	43 (7.3)	10 (9.3)	
HTN				<0.001
No	391 (55.9)	354 (59.8)	37 (34.3)	
Yes	309 (44.1)	238 (40.2)	71 (65.7)	
CVD				0.003
No	410 (58.6)	361 (61.0)	49 (45.4)	
Yes	290 (41.4)	231 (39.0)	59 (54.6)	
Antithromb Use				0.021
No	417 (59.6)	364 (61.5)	53 (49.1)	
Yes	283 (40.4)	228 (38.5)	55 (50.9)	
GC Route				0.828
Systemic	360 (51.4)	305 (51.5)	55 (50.9)	
Inhaled	141 (20.1)	121 (20.4)	20 (18.5)	
None	199 (28.4)	166 (28.0)	33 (30.6)	
Statin use				0.016
No	481 (68.7)	418 (70.6)	63 (58.3)	
Yes	219 (31.3)	174 (29.4)	45 (41.7)	
Age	78.00 [69.00, 84.00]	77.00 [69.00, 84.00]	81.00 [71.25, 85.00]	0.048
LOS days	9.00 [7.00, 13.00]	9.00 [7.00, 13.00]	9.00 [6.00, 16.00]	0.645
COPD Duration	10.00 [5.00, 11.25]	10.00 [5.00, 10.00]	10.00 [5.00, 20.00]	0.077
SBP(mmHg)	137.00 [122.00, 154.00]	136.00 [120.00, 153.25]	139.50 [128.00, 154.25]	0.048
GC Days	6.00 [0.00, 10.00]	6.00 [0.00, 10.00]	4.00 [0.00, 9.25]	0.288
WBC ($\times 10^9/L$)	7.87 [6.23, 10.75]	7.85 [6.22, 10.85]	8.04 [6.39, 10.12]	0.888
N ($\times 10^9/L$)	5.69 [4.05, 8.42]	5.66 [4.09, 8.52]	5.83 [3.95, 8.30]	0.671
LYM ($\times 10^9/L$)	1.13 [0.76, 1.62]	1.12 [0.75, 1.61]	1.27 [0.80, 1.67]	0.158
MON ($\times 10^9/L$)	0.64 [0.43, 0.83]	0.64 [0.43, 0.83]	0.66 [0.45, 0.84]	0.601
HB (g/L)	125.45 [113.00, 138.80]	124.90 [113.07, 138.00]	127.25 [111.78, 141.25]	0.338
HCT (%)	38.30 [34.40, 42.20]	38.20 [34.40, 42.10]	38.85 [34.88, 42.90]	0.586
PLT ($\times 10^9/L$)	210.00 [168.68, 260.45]	208.00 [168.00, 258.02]	221.30 [175.25, 277.30]	0.212
PCT (ng/mL)	0.09 [0.02, 0.20]	0.08 [0.02, 0.19]	0.13 [0.03, 0.22]	0.011
ALT (U/L)	15.10 [10.60, 23.50]	15.00 [10.50, 22.95]	15.65 [11.00, 24.40]	0.403
K (mmol/L)	4.02 [3.72, 4.34]	4.01 [3.72, 4.33]	4.08 [3.74, 4.42]	0.258
Na (mmol/L)	140.10 [137.50, 142.10]	140.10 [137.30, 142.10]	140.05 [138.20, 142.20]	0.456
UA ($\mu\text{mol/L}$)	299.55 [223.28, 384.30]	297.00 [221.73, 376.18]	318.72 [238.45, 422.75]	0.077
HDL (mmol/L)	1.39 [1.10, 1.69]	1.41 [1.13, 1.71]	1.28 [0.98, 1.56]	0.001

(Continued)

Table 2 (Continued).

Variables	Total (n = 700)	No DM (n = 592)	DM (n = 108)	P value
LDL (mmol/L)	2.43 [1.86, 3.17]	2.40 [1.85, 3.14]	2.55 [1.98, 3.42]	0.156
eGFR (mL/min/1.73 m ²)	82.80 [66.27, 93.38]	82.88 [66.91, 93.32]	81.53 [63.12, 95.49]	0.879
APTT (s)	33.60 [28.78, 38.80]	33.90 [29.30, 39.12]	31.85 [26.67, 36.50]	<0.001
FIB (g/L)	3.75 [2.96, 4.57]	3.73 [2.95, 4.55]	3.88 [3.00, 4.57]	0.426
TyG	8.16 [7.88, 8.50]	8.11 [7.84, 8.42]	8.53 [8.15, 8.95]	<0.001
PNI	42.75 [39.04, 46.95]	42.75 [39.10, 46.71]	42.65 [38.61, 47.50]	0.859

Abbreviations: HTN, hypertension; CVD, cardiovascular disease; Antithromb Use, use of anticoagulants and/or antiplatelet agents; GC Route, route of glucocorticoid administration at the index hospitalization (none indicates no glucocorticoid use; inhaled includes inhaled corticosteroids and nebulized inhaled glucocorticoids); systemic indicates oral or intravenous glucocorticoids; Statin Use, statin use; LOS days, length of hospital stay; SBP, systolic blood pressure; GC Days, duration of glucocorticoid use; WBC, white blood cell count; N, neutrophil count; LYM, lymphocyte count; MON, monocyte count; HB, hemoglobin; HCT, hematocrit; PLT, platelet count; PCT, procalcitonin; ALT, alanine aminotransferase; K, serum potassium; Na, serum sodium; UA, uric acid; HDL, high-density lipoprotein; LDL, low-density lipoprotein; eGFR, estimated glomerular filtration rate; APTT, activated partial thromboplastin time; FIB, fibrinogen; TyG, triglyceride–glucose index; PNI, prognostic nutritional index. TyG = $\ln [TG (mg/dL) \times FPG (mg/dL) / 2]$; TG and FPG measured in mmol/L were converted to mg/dL before calculation ($TG \times 88.57$; $FPG \times 18.0$). PNI = albumin (g/L) + 5 × lymphocyte count ($10^9/L$).

Multifactorial Logistic Analysis

Univariable and multivariate logistic regression showed that HTN and TyG were related to a higher risk of new-onset T2DM, whereas HDL and APTT showed protective effects. (Table 3).

Table 3 Univariable and Multivariable Logistic Regression Analyses in the Training Set

Variables	Univariable OR (95% CI)	Univariable P value	Multivariable OR (95% CI)	Multivariable P value
Sex	0.758 (0.487–1.200)	0.226	—	—
Smoking history	0.806 (0.523–1.227)	0.321	—	—
Alcohol drinking history	1.303 (0.601–2.580)	0.472	—	—
HTN	2.854 (1.868–4.425)	<0.001	2.148 (1.345–3.466)	0.002
CVD	1.882 (1.246–2.853)	0.003	1.541 (0.933–2.547)	0.091
Antithromb Use	1.657 (1.097–2.505)	0.016	0.954 (0.537–1.676)	0.872
GC Route	—	0.828	—	—
Statin use	1.716 (1.121–2.610)	0.012	1.103 (0.623–1.950)	0.736
Age	1.019 (0.998–1.040)	0.084	—	—
LOS days	1.013 (0.993–1.032)	0.183	—	—
COPD Duration	1.020 (1.000–1.039)	0.041	1.016 (0.994–1.037)	0.143
SBP(mmHg)	1.000 (0.996–1.002)	0.887	—	—
GC Days	0.989 (0.957–1.018)	0.474	—	—
WBC ($\times 10^9/L$)	0.992 (0.940–1.041)	0.747	—	—
N ($\times 10^9/L$)	0.986 (0.934–1.036)	0.602	—	—
LYM ($\times 10^9/L$)	1.213 (0.914–1.589)	0.169	—	—
MON ($\times 10^9/L$)	1.136 (0.607–2.085)	0.685	—	—
HB (g/L)	1.006 (0.996–1.015)	0.255	—	—
HCT (%)	1.004 (0.975–1.034)	0.805	—	—
PLT ($\times 10^9/L$)	1.001 (0.999–1.004)	0.326	—	—
PCT (ng/mL)	1.067 (0.991–1.176)	0.114	—	—
ALT (U/L)	0.999 (0.995–1.001)	0.620	—	—
K (mmol/L)	1.235 (0.839–1.808)	0.280	—	—
Na (mmol/L)	1.014 (0.972–1.061)	0.531	—	—
UA ($\mu\text{mol/L}$)	1.002 (1.000–1.003)	0.058	—	—
HDL (mmol/L)	0.462 (0.288–0.726)	0.001	0.531 (0.312–0.877)	0.016
LDL (mmol/L)	1.245 (1.043–1.498)	0.016	1.054 (0.853–1.284)	0.607

(Continued)

Table 3 (Continued).

Variables	Univariable OR (95% CI)	Univariable P value	Multivariable OR (95% CI)	Multivariable P value
eGFR (mL/min/1.73 m ²)	0.999 (0.991–1.009)	0.908	—	—
APTT (s)	0.951 (0.927–0.975)	<0.001	0.956 (0.930–0.982)	0.001
FIB (g/L)	1.023 (0.903–1.135)	0.673	—	—
TyG	3.474 (2.463–4.988)	<0.001	2.772 (1.906–4.098)	<0.001
PNI	0.993 (0.962–1.024)	0.642	—	—

Notes: TyG = $\ln [\text{TG (mg/dL)} \times \text{FPG (mg/dL)} / 2]$; TG and FPG measured in mmol/L were converted to mg/dL before calculation ($\text{TG} \times 88.57$; $\text{FPG} \times 18.0$). PNI = albumin (g/L) + 5 × lymphocyte count ($10^9/\text{L}$).

Abbreviations: HTN, hypertension; CVD, cardiovascular disease; Antithromb Use, use of anticoagulants and/or antiplatelet agents; GC Route, route of glucocorticoid administration at the index hospitalization (none indicates no glucocorticoid use; inhaled includes inhaled corticosteroids and nebulized inhaled glucocorticoids); systemic indicates oral or intravenous glucocorticoids; Statin Use, statin use; LOS days, length of hospital stay; SBP, systolic blood pressure; GC Days, duration of glucocorticoid use; WBC, white blood cell count; N, neutrophil count; LYM, lymphocyte count; MON, monocyte count; HB, hemoglobin; HCT, hematocrit; PLT, platelet count; PCT, procalcitonin; ALT, alanine aminotransferase; K, serum potassium; Na, serum sodium; UA, uric acid; HDL, high-density lipoprotein; LDL, low-density lipoprotein; eGFR, estimated glomerular filtration rate; APTT, activated partial thromboplastin time; FIB, fibrinogen; TyG, triglyceride–glucose index; PNI, prognostic nutritional index.

Feature Selection via LASSO Regression

In the training cohort, all baseline variables were included in a LASSO logistic regression model. The coefficient profiles across the $\log(\lambda)$ sequence are shown in [Figure 1A](#). We used 10-fold cross-validation to select the tuning parameter λ ([Figure 1B](#)). At $\lambda_{\min}$, six variables retained non-zero regression coefficients: HTN, CVD, HDL, APTT, TyG, and PCT [Figure 1A](#). To derive a parsimonious model and enhance clinical applicability, the final nomogram was constructed using the four predictors with the largest absolute LASSO coefficients (HTN, CVD, HDL, and TyG).

Nomogram Construction

Based on four predictors selected by LASSO (HTN, CVD, HDL, and TyG), we developed a nomogram to estimate the five-year probability of new-onset T2DM among COPD patients ([Figure 2](#)). In this nomogram, each predictor was given a point score based on its regression coefficient. Higher total points indicate a higher estimated five-year probability of T2DM.

Model Performance and Clinical Utility

The model achieved AUCs of 0.749, 0.758, and 0.798 in the training, internal validation, and external validation, respectively ([Figure 3](#)). Calibration curves indicated that predicted probabilities were in line with the observed event rates in both the training and internal validation cohorts, with similar performance in the external cohort ([Figure 4](#)). Using the optimal probability threshold derived from the internal validation cohort, the model maintained comparable sensitivity and specificity in all cohorts

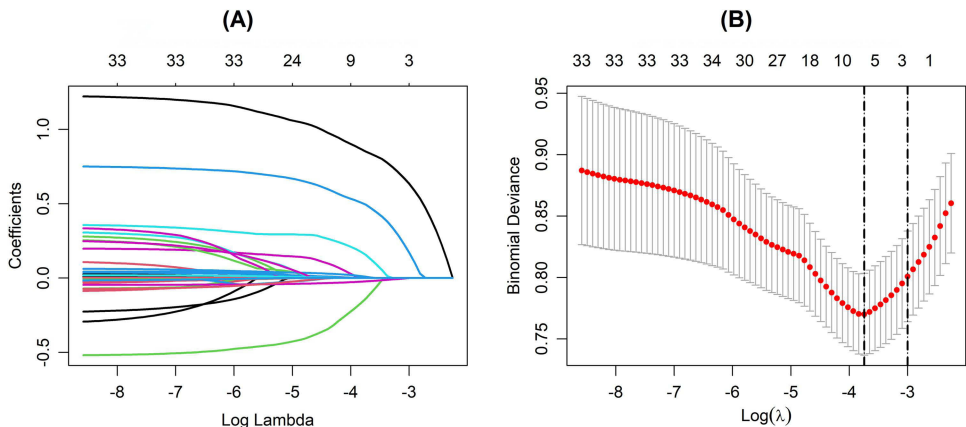


Figure 1 LASSO feature selection for the nomogram. **(A):** Coefficient profiles of candidate predictors across the $\log(\lambda)$ sequence in the training set. Each colored curve represents one candidate predictor; the numbers above the plot indicate the number of predictors with non-zero coefficients at each λ . **(B):** Ten-fold cross-validation for λ selection. Dashed vertical lines indicate $\lambda_{\min}$ and λ_{1se} .

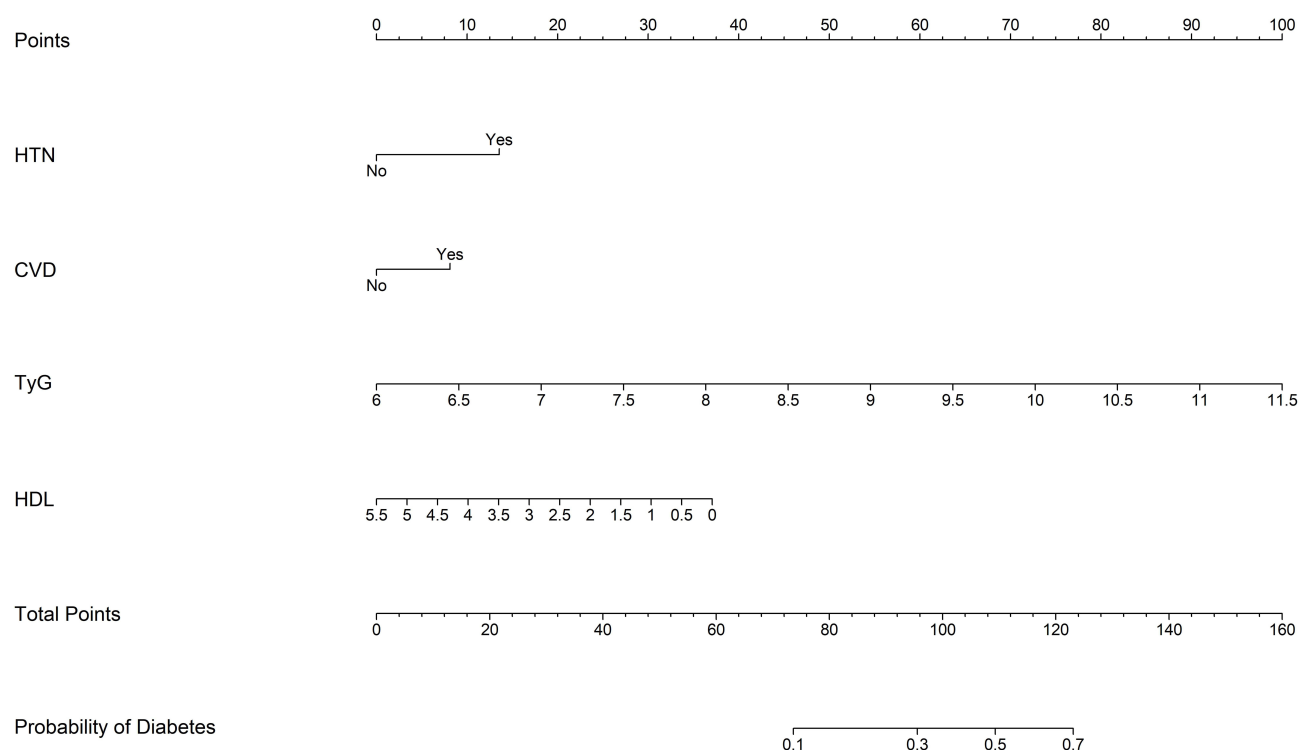


Figure 2 Nomogram for predicting the 5-year risk of new-onset T2DM in patients with COPD. The nomogram includes hypertension (HTN), cardiovascular disease (CVD), triglyceride-glucose index (TyG), and high-density lipoprotein (HDL). Points for each predictor are summed to obtain the total score, corresponding to the predicted 5-year risk.

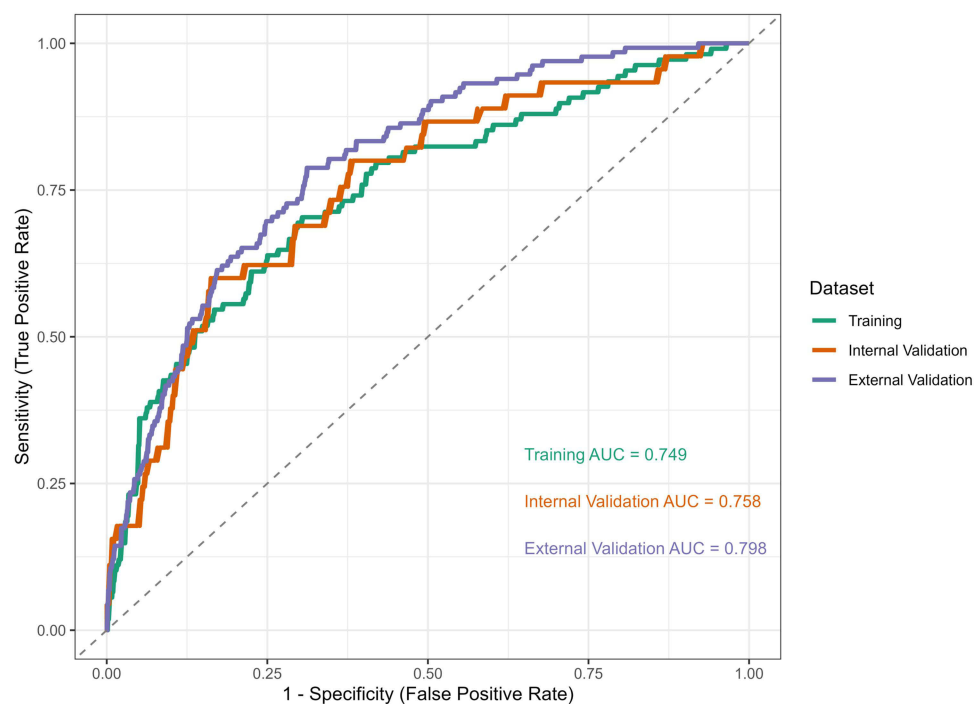


Figure 3 ROC curves of the nomogram for predicting 5-year new-onset T2DM in patients with COPD. The AUCs were 0.749 (training), 0.758 (internal validation), and 0.798 (external validation). The diagonal dashed line indicates no discrimination.

(Table 4). DCA supported the clinical utility of the nomogram, with net clinical benefit exceeding treat-all or treat-none from 5% to 50% thresholds (Figure 5). In the internal validation cohort, subgroup analyses stratified by sex, age, and hypertension status showed similar discrimination across subgroups (Figure 6).

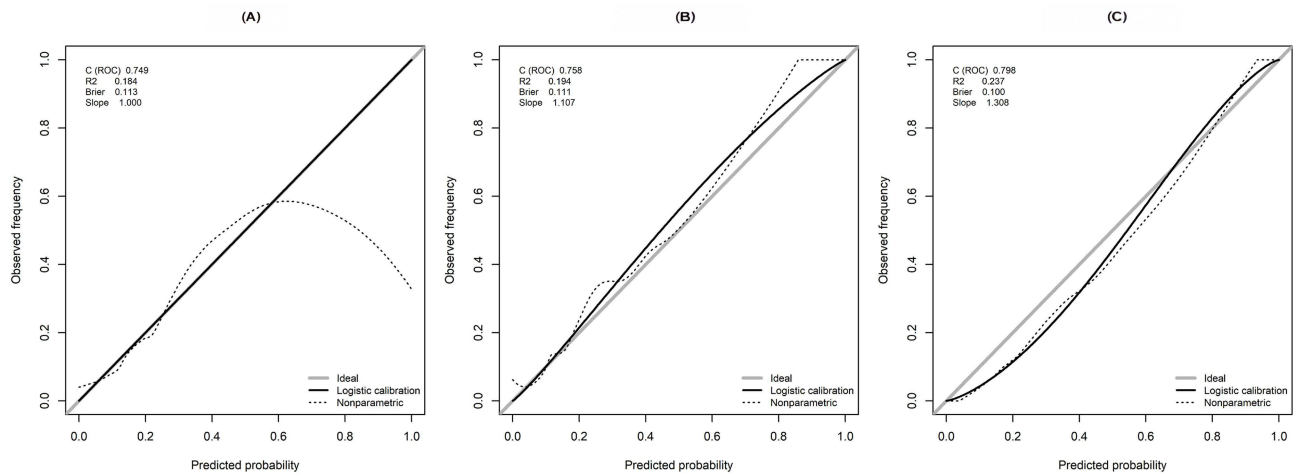


Figure 4 Calibration curves of the nomogram for predicting 5-year new-onset diabetes in patients with COPD. **(A)** Training cohort; **(B)** internal validation cohort; **(C)** External validation cohort. The grey 45-degree line indicates ideal calibration. The solid line indicates the calibration curve of the current model, and the dotted line indicates the nonparametric calibration curve. Across the three cohorts, the calibration curves show the agreement between predicted probabilities and observed event frequencies.

Discussion

COPD is a chronic airway disorder with systemic consequences. Globally, COPD ranks as the fourth most common cause of death.²⁸ Compared with the general population, patients with COPD show a higher incidence of T2DM.²⁹ This not only increases the disease burden but is also associated with higher mortality rates, poor prognosis, and significantly reduces patients’ quality of life.³⁰ Therefore, developing a risk prediction tool based on simple clinical indicators may enable clinicians to identify patients at higher metabolic risk earlier and improve long-term outcomes. In this study, we used retrospective cohort data from two hospitals to develop and validate a nomogram for 5-year incident T2DM among COPD inpatients without baseline diabetes. The final model included four predictors: TyG, HTN, CVD, and HDL. Unlike previous cross-sectional studies, our work focused on COPD patients who have not yet been diagnosed with diabetes, providing a new tool for early identification and follow-up of potentially high-risk patients.

Evidence regarding the association between ICS and incident /dysglycaemia T2DM in patients with COPD has been mixed. While some observational studies suggest an increased risk with high-dose ICS exposure, post hoc analyses of randomized trials, meta-analyses and some real-world studies have not shown a consistent association.^{31,32} In our study, baseline glucocorticoid route at the index hospitalization was not significantly associated with incident T2DM during follow-up. Notably, glucocorticoid exposure was ascertained only from medication records at admission and during the index hospitalization. Information on post-discharge long-term maintenance inhaler therapy, cumulative dose, and adherence was not collected. Therefore, we were unable to evaluate long-term exposure patterns or potential dose-response relationships. In addition, the high comorbidity burden and complex concomitant treatments in hospitalized COPD patients may further complicate assessment of the independent metabolic effect of ICS. Therefore, future studies with more complete longitudinal data on ICS exposure are warranted to better clarify its association with incident diabetes.

TyG reflects insulin resistance (IR) and is readily obtainable from routine laboratory tests.³³ Prior studies suggest that TyG may perform better for T2DM risk prediction than either fasting glucose or triglycerides alone, with potentially

Table 4 Predictive Performance Analysis of the 5-Year New-Onset Diabetes Nomogram for Chronic Obstructive Pulmonary Disease (COPD) Patients

Data	N (Events)	Accuracy (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Training	700 (108)	0.75 (0.72–0.78)	0.57 (0.48–0.67)	0.78 (0.75–0.81)
Internal validation	298 (45)	0.80 (0.75–0.84)	0.60 (0.44–0.74)	0.84 (0.79–0.88)
External validation	1018 (132)	0.67 (0.64–0.70)	0.80 (0.72–0.87)	0.65 (0.62–0.68)

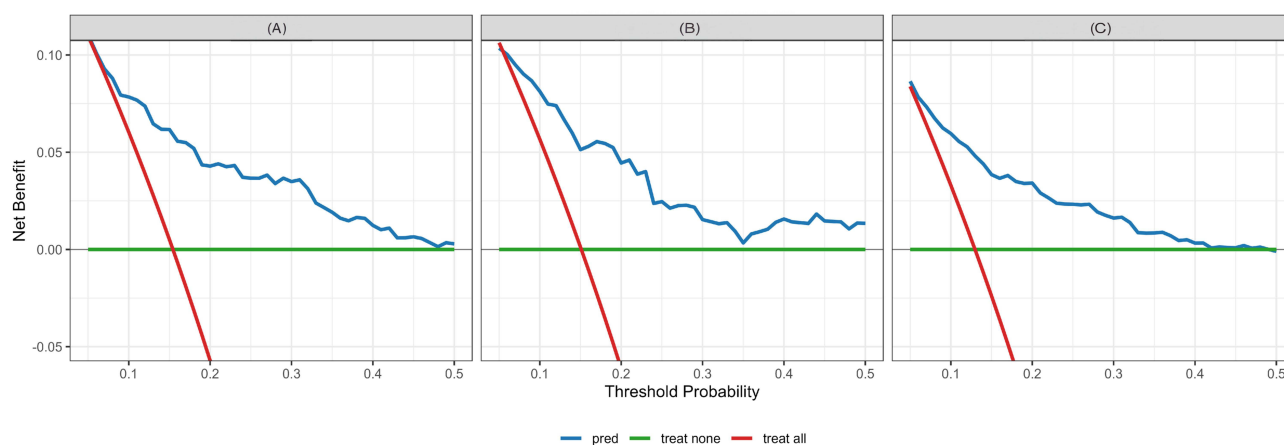


Figure 5 DCA of the nomogram for predicting 5-year new-onset diabetes in patients with COPD. (A) Training cohort; (B) Internal validation cohort; (C) External validation set. The x-axis indicates the threshold probability, and the y-axis indicates the net benefit. The nomogram is compared with the treat-all and treat-none strategies.

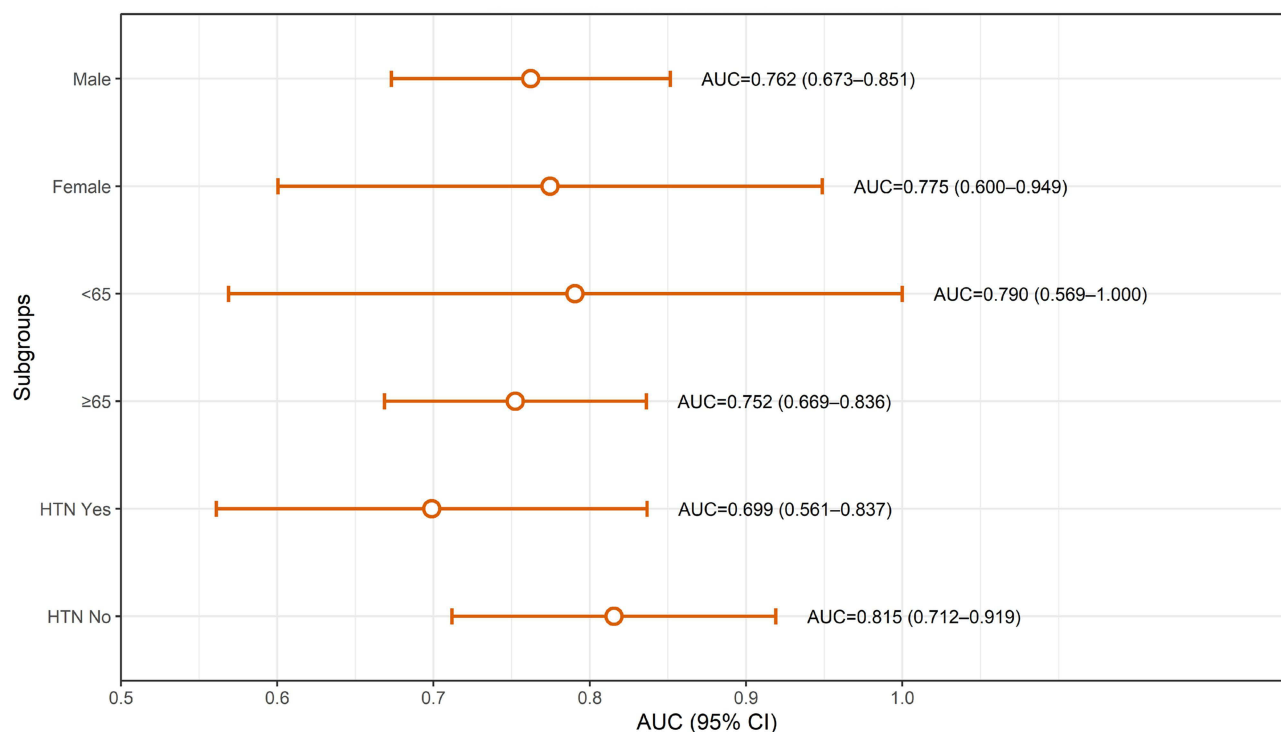


Figure 6 Subgroup analysis of the 5-Year New-Onset Diabetes Nomogram in COPD Patients (internal validation). AUCs with 95% confidence intervals for the nomogram across subgroups defined by sex, age, and hypertension status.

greater utility in non-obese individuals.^{34–36} This may apply to COPD, as TNF- α and IL-6 elevation, malnutrition, and muscle loss can contribute to IR.³⁷ Prospective cohorts suggest that higher TyG levels are linked to more frequent COPD events and poorer outcomes.^{38,39} In our cohort, TyG emerged as the most informative independent predictor of new-onset T2DM in COPD. This suggests that incorporating TyG into routine COPD assessment may improve early risk stratification and support closer glycaemic monitoring in high-risk patients.

In our study, new-onset T2DM occurred more often among COPD patients with HTN or CVD. Hypertension is an early manifestation of metabolic abnormalities and has been linked to a higher risk of new-onset T2DM. A large British prospective cohort study reported that patients with higher systolic blood pressure was more likely to develop T2DM.⁴⁰ This may imply

that blood pressure may coexist with early abnormalities in blood glucose, possibly through inflammation and sympathetic activation. In COPD patients, this effect may be amplified.^{41,42} Various cardiovascular diseases may also accelerate the progression of T2DM. Coronary artery disease may increase the likelihood of developing diabetes. Endothelial injury and metabolic stress are possible contributors.^{43,44} In a cohort of patients with acute myocardial infarction (AMI), about 23% developed diabetes within five years.⁴⁵ Similar risks have also been reported in patients with heart failure.^{46,47} These findings suggest that cardiovascular disease may accelerate metabolic deterioration. Moreover, the CVD2DM model developed by Helmkink suggested that the risk of new-onset T2DM remains substantial even with guideline-directed cardiovascular therapy.⁴⁸ Statins are commonly used for secondary prevention in patients with CVD, but they may increase the risk of diabetes, adding to the metabolic burden.^{49,50} Our findings indicate that long-term management of COPD cannot rely only on respiratory care. For patients with concomitant HTN and CVD, systematic assessment and follow-up of glucose metabolism beyond routine cardiovascular risk stratification may help delay the onset of T2DM.

HDL not only regulates lipid metabolism but also participates in anti-inflammation, antioxidant defense, and glucose metabolism.^{51,52} Low HDL levels were consistently related to T2DM, IR, and glucose intolerance.⁵³ In a double blind, placebo-controlled crossover trial, Drew et al found that short-term recombinant HDL therapy improved glycemic control and β -cell function,⁵⁴ indicating that HDL may have metabolic benefits. In COPD patients, chronic systemic inflammation may compromise the structure and function of HDL,^{55,56} so that even normal HDL plasma concentrations may not provide adequate protection and could facilitate progression to diabetes. Existing diabetes risk prediction models in the general population have identified low HDL as a strong predictor, second only to abnormal fasting blood glucose levels.⁵⁷ Similarly, in our analysis, low HDL emerged as a risk marker for new-onset T2DM in COPD and showed stable contribution to the nomogram. We consider that incorporating HDL levels and their dynamic changes into long term COPD follow-up, combined with lifestyle intervention, may not only reduce cardiovascular events risk but also improve patients' glucose metabolism.

Notably, a relatively high proportion of participants in our cohort were never-smokers and women. This pattern may reflect the epidemiological characteristics of COPD in Guangdong. In the Chinese population, COPD among never-smokers is not uncommon and the proportion of never-smokers is substantially higher among women.^{58,59} Beyond tobacco exposure, non-tobacco factors including indoor and ambient air pollution, secondhand smoke exposure, occupational dust exposure, and household cooking emissions or biomass fuel smoke may contribute substantially to the development and progression of COPD, particularly among women.

Most previous work is cross-sectional and often focuses on patients with established diabetes or acute COPD exacerbations, which limits the value for long-term clinical management. We therefore followed COPD patients without diabetes at baseline for five years and developed a nomogram using routine clinical variables. The nomogram showed good discrimination in different cohorts. Calibration analysis suggested that predicted risks were generally consistent with the observed event frequencies. DCA plots indicated the clinical utility within a reasonable range of threshold probabilities. Subgroup analyses by age, sex and hypertension showed similar performance, supporting generalizability. In routine follow-up of COPD, TyG, HTN, CVD and HDL can be used as a simple risk check to identify patients at higher risk of T2DM. For patients at higher risk, COPD care should extend beyond respiratory management to include periodic checks of glucose, blood pressure, and lipid profiles to support metabolic risk control.

However, this study has some limitations. First, this retrospective cohort design meant that some clinical data, such as C-reactive protein (CRP) and glycated hemoglobin, were incompletely recorded in the EMR and were not included. In addition, spirometry reports were available only for a subset of patients, Spirometry-based GOLD severity indicators such as FEV1% predicted, GOLD grade could not be comprehensively assessed. This may have limited objective confirmation of airflow obstruction and evaluation of the impact of COPD severity on incident T2DM. Follow-up information was mainly on medical records and telephone interviews, so some T2DM events may not have been captured, and the incidence may be underestimated. In addition, the number of new-onset T2DM events was limited, leading to class imbalance. Despite the modest number of events, the events-per-variable (EPV) was acceptable, and model performance remained consistent in the external validation and subgroup analyses. However, a larger cohort is still needed to validate these findings. Finally, because this cohort was drawn from hospitals in Guangdong, the findings may not fully generalize to other populations. Larger multicenter studies in different regions are warranted to validate and refine the nomogram.

Conclusion

In summary, we developed and externally validated a nomogram to estimate the five-year risk of new-onset T2DM in COPD using four routine variables (TyG, HTN, CVD, and HDL). The nomogram achieved good discrimination and acceptable calibration, with potential clinical usefulness on decision-curve analysis. This tool may support risk stratification during follow-up and help prioritize metabolic monitoring in patients at higher risk. Prospective multicenter studies are needed to validate these findings.

Abbreviations

T2DM, Type 2 diabetes mellitus; COPD, chronic obstructive pulmonary disease; LASSO, least absolute shrinkage and selection operator; ROC, Receiver Operating Characteristic; AUC, Area Under the Receiver Operating Characteristic Curve; DCA, Decision Curve Analysis; GOLD, Global Initiative for Chronic Obstructive Lung Disease; ADA, American Diabetes Association; EMR, Electronic Medical Record; MICE, Multivariate Imputation by Chained Equations; SD, Standard Deviation; IQR, Interquartile Range; IR, Insulin Resistance; AMI, Acute Myocardial Infarction; CRP, C-reactive Protein; OR, Odds Ratio; CI, Confidence Interval; HTN, hypertension; CVD, cardiovascular disease; Antithromb Use, use of anticoagulants and/or antiplatelet agents; GC Route, route of glucocorticoid administration (systemic indicates oral or intravenous glucocorticoids); Statin Use, statin use; LOS days, length of hospital stay; SBP, systolic blood pressure; GC Days, duration of glucocorticoid use; WBC, white blood cell count; N, neutrophil count; LYM, lymphocyte count; MON, monocyte count; HB, hemoglobin; HCT, hematocrit; PLT, platelet count; PCT, procalcitonin; ALT, alanine aminotransferase; K, serum potassium; Na, serum sodium; UA, uric acid; HDL, high-density lipoprotein; LDL, low-density lipoprotein; eGFR, estimated glomerular filtration rate; APTT, activated partial thromboplastin time; FIB, fibrinogen; TyG, triglyceride–glucose index; PNI, prognostic nutritional index.

Ethical Approval

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committees of the Affiliated Hospital of Guangdong Medical University and the Second Affiliated Hospital of Guangdong Medical University (Ethics number: PJKT2025-096 and PJKT2025-045). The requirement for informed consent was waived because the study used anonymized retrospective data.

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Author Contributions

All authors made a significant contribution to the work reported, whether 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

All authors declare no competing interests in this study.

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