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Establishing and internally validating a predictive model for coronary heart disease incorporating triglyceride-glucose index, monocyte-to-high-density lipoprotein cholesterol ratio and conventional risk factors in patients experiencing chest pain and referred for invasive coronary angiography

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Abstract

Background Coronary heart disease (CHD) represents a severe form of ischemic cardiac condition that necessitates timely and accurate diagnosis. Although coronary angiography (CAG) remains widely used to detect CHD, healthcare facilities, medical expenses, and equipment technology often limit its availability. Therefore, it is imperative to identify a non-invasive diagnostic approach with high accuracy for CHD.

Methods This cross-sectional research included patients with chest pain (≥ 18 years) hospitalized at Chengde Central Hospital between September 2020 and March 2024. Among the participants, 70% were split into the training, and 30% were randomly entered into the validation sets. In the training dataset, univariate and multivariate logistic regression analyses were rigorously employed to ascertain predictors of CHD. A model was formulated by incorporating these predictors in a nomogram, which was evaluated for accuracy using calibration curves. The

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model's discrimination was quantified by calculating the area under the receiver operating characteristic (ROC) curve, denoted as the area under the curve (AUC), and its clinical application value was determined through decision curve analysis (DCA). Finally, we compare our model against the pretest probability (PTP) calculated by the Update Diamond-Forrester Model (UDFM) as recommended by the ECS guidelines to comprehensively assess its performance.

Results This study included 1501 patients who presented with chest pain, with a mean age of 60.45 years, 865 males (57.60%). Multivariate logistic regression analysis revealed TyG index, MHR, male, age, diabetes, systolic blood pressure (SBP), regional wall motion abnormality (RWMA), ST-T changes, and low-density lipoprotein cholesterol (LDL-C) as independent predictors of CHD. A novel nomogram incorporating these independent risk factors exhibited high accuracy and perfect consistency, with a training set AUC calculated to be 0.733 (95% CI: 0.698–0.768), and the validation set maintained a strong performance at 0.721 (95% CI: 0.663–0.779). The calibration curves and the Hosmer-Lemeshow test confirmed the well-fitting model ($P=0.576$ and $P=0.694$). ROC curve analysis and DCA demonstrated that the model has robust forecasting capability.

Conclusion The nomogram model in this study exhibited good discriminative ability, calibration, and a favorable net benefit. Its predictive performance exceeds that of the traditional PTP tool and may serve as a non-invasive and promising approach to aid clinicians in the early identification of CHD risk in patients presenting with chest pain.

Keywords Coronary heart disease, Predictive model, Triglyceride-glucose index, Monocyte-to-high-density lipoprotein cholesterol ratio

Introduction

CHD, characterized by high morbidity and mortality rates, has become a severe global public health problem [1]. With approximately 11.39 million people affected, China has the most significant prevalence of CHD worldwide, a number expected to rise to 22.63 million by 2030, imposing a substantial economic burden on society and patients [2, 3]. Diamond and Forrester first introduced the Diamond-Forrester Model (DFM) in 1979, highlighting the importance of PTP in the diagnosis of CHD. They developed a simple, rapid, and clinically practical model that incorporated three key factors: age, sex, and chest pain type [4]. However, as subsequent research progressed, it became apparent that PTP often overestimated the risk of CHD [5]. Early detection of individuals with an elevated risk of CHD is crucial for providing timely treatments, which can contribute to the reduction of the occurrence and severity of CHD-related complications. While CAG remains the gold standard for CHD diagnosis, its high costs and associated risks limit its widespread use for screening. Therefore, developing a non-invasive predictive model to predict CHD risk in patients is essential.

In recent years, numerous researchers have focused on identifying reliable biomarkers for early recognition of CHD. Although several biomarkers are currently employed for CHD diagnosis and prediction, their effectiveness remains suboptimal. The pathological basis of CHD involves the formation of arterial atherosclerosis, which is primarily driven by the inflammatory reaction. Insulin resistance (IR) can activate proinflammatory pathways and cytokines release and exacerbate plaque formation. The TyG index is a valuable alternative IR indicator representing a substantial risk indicator for arterial stiffness [6–8].

Additionally, monocytes, a crucial white blood cell, contribute to atherosclerotic plaque formation through endothelial dysfunction, arterial injury, and systemic or localized inflammatory responses that damage coronary arteries [9]. High-density lipoprotein cholesterol(HDL-C), called 'good cholesterol,' facilitates the removal of surplus cholesterol from the circulatory system and directs it toward the liver for subsequent excretion. Furthermore, HDL-C possesses significant antioxidant, anti-inflammatory, and anti-atherosclerotic advantages [10]. The monocyte-to-high-density lipoprotein cholesterol ratio (MHR) is an emerging biomarker that indicates systemic inflammatory equilibrium and is significantly linked to the risk of CHD [11]. However, few studies have established and validated predictive models for CHD risk incorporating the TyG index and MHR. This investigation aims to construct a novel, non-invasive CHD prediction model by incorporating conventional risk factors, the TyG index, and MHR and assess its predictive efficiency.

Methods

Study participants

This study is based on cross-sectional data collection. A total of 1,866 patients with chest pain suspected of having CHD were consecutively enrolled from the cardiovascular department of Chengde City Central Hospital between September 2020 and March 2024. The inclusion criteria were as follows: (1) patients admitted to the cardiovascular department due to chest tightness or chest pain; (2) absence of acute infection, hyperthyroidism, severe renal dysfunction, or contrast allergies; (3) patients

aged ≥ 18 years; (4) patients agreed to sign informed consent. Exclusion criteria included: (1) individuals with a history of CHD or prior revascularization; (2) complicated with other heart diseases (such as congenital heart disease, severe valvular heart disease, etc.); (3) patients who did not complete the CAG. The research was performed strictly with the terms of the Declaration of Helsinki, which emphasizes the importance of ethics. It was also sanctioned by the Ethics Committee of Chengde City Central Hospital, with every participant providing informed consent. Fig. 1 illustrates the trial procedure.

This prediction model study follows the TRIPOD checklist [12]. The Chinese clinical registration identifier for this trial is ChiCTR2000041499, which is accessible online at http://www.chictr.org.cn.

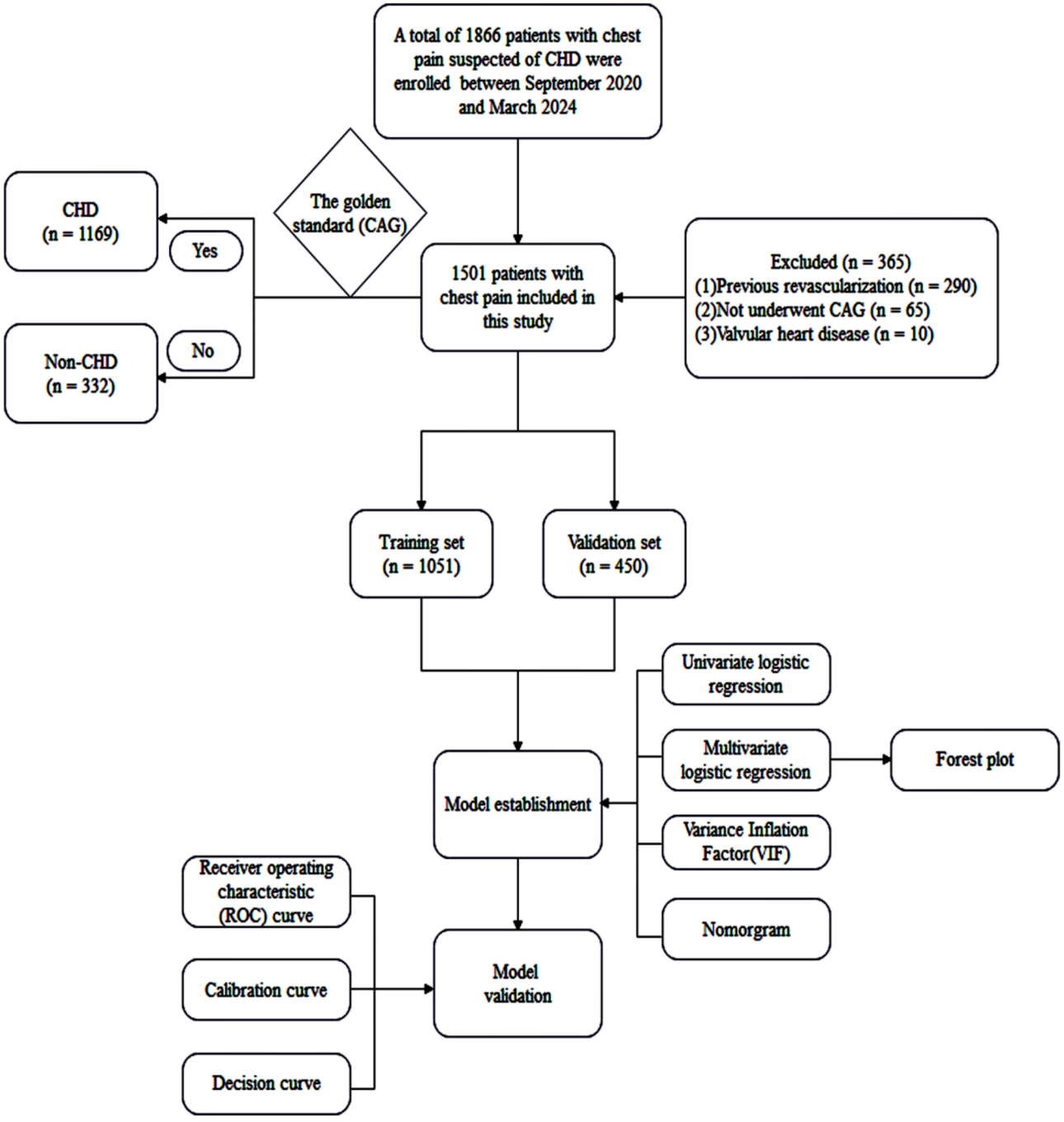

Fig. 1 Flowchart of the trial. Abbreviations: CHD, Coronary heart disease; CAG, Coronary angiography; ROC, Receiver operating characteristic; VIF, Variance inflation factor

Data collection and definition

Based on previous publications and biological considerations, we collected a comprehensive set of covariates known to confound CHD outcomes wherever possible. On the day of admission, extensive data, including gender, age, medical history, family history of CHD, diabetes, and habits related to alcohol consumption and smoking, were meticulously collected and documented through a thorough medical history inquiry. Patients' weight and height were measured while wearing minimal attire and without shoes. The standard formula weight (kg)/square of height (m^2) was used to figure out body mass index (BMI). After 5 min of rest, an automatic manometer was used to measure blood pressure in the right arm. Serum levels of total cholesterol (TC), triglyceride (TG), fasting plasma glucose (FPG), and other parameters were examined with a sophisticated, automated biochemical analyzer (HITACHI 7600, Japan) after a minimum 8 h fast. Additionally, red blood cell count (RBC), monocyte count (Mono), etc., were determined via an XS-500i automated hematology analyzer (Sysmex Corporation, Kobe, Japan). All participants underwent the resting-state electrocardiogram and the echocardiogram. All the tests above were conducted before the patient underwent CAG and adhered strictly to the relevant guidelines and regulations. Subsequently, the outcomes were meticulously reviewed and documented through the electronic medical record (EMR) system by two independent physicians unaware of the patient's personal information. To minimize errors, senior physicians verified the data.

The definition of hypertension is systolic blood pressure (SBP) exceeding 139 mmHg, diastolic blood pressure (DBP) exceeding 89 mmHg, or taking blood pressure lowering medications [13]. Diabetes is diagnosed based on the diagnostic criteria developed by the WHO Diabetes Mellitus Expert Committee [14]. Hyperlipidaemiais diagnosed based on the most recent lipid management guidelines in China [15]. The diagnosis of hyperuricemia is confirmed in male individuals with fasting serum uric acid concentrations surpassing 420 μmol/L on two separate occasions under a normal purine diet. For females, the diagnostic threshold is 360 μmol/L [16]. ST-T changes are diagnosed according to the criteria: ST segment depression exceeding 0.05 millivolts, T-wave inversions, T- to R-wave amplitude ratio < 1:10, and electrocardiographic normalization occurs following symptomatic relief [17].

The computation of the TyG index for each participant was conducted by employing a specific mathematical formula: ln[TG (mg/dL) × FPG (mg/dL)/2] [18]. The MHR was achieved by dividing the monocyte count ($\times 10^9$/L) by the concentration of HDL-C (mmol/L) [19].

Coronary angiography

Selective multiposition CAG was performed in the catheterization room by proficient interventional physicians following the Judkins method via femoral or radial artery access. At least two experienced interventional cardiologists assessed the angiographic findings. In cases of disagreement, a third physician was consulted to achieve consensus. CHD was diagnosed if ≥ 50% diameter stenosis was observed in any epicardial coronary artery or its principal branches based on CAG results. The rationale behind this definition is that when coronary artery stenosis reaches 50%, the lumen area is significantly reduced, resulting in a marked decrease in blood flow distal to the stenosis. During physical exertion or increased myocardial oxygen demand, the myocardium's oxygen supply becomes insufficient, leading to noticeable clinical symptoms of myocardial ischemia. Furthermore, the 50% stenosis threshold offers higher sensitivity, facilitating the early detection of patients at risk for CHD [20, 21].

Logistic regression analysis and nomogram model development

The subjects were randomized into two separate cohorts. The initial cohort, designated as the training set, comprised 1051 subjects, accounting for 70% of the total sample size. The remaining 30% of the sample, totaling 450 subjects, formed the validation set [22]. All extracted variables had missing values below 20%, and these missing values were handled using multiple imputation [23]. The risk of CHD was visually represented using a nomogram. Firstly, to identify contributory risk factors for CHD among individuals experiencing chest pain, univariate logistic regression analysis was meticulously conducted on the designated training cohort. Subsequently, covariates demonstrating statistical significance ($P < 0.05$) from the univariate logistic regression were advanced to a backward stepwise multivariate logistic regression to ascertain significant predictors for the nomogram.

Performance of the nomogram model

The performance of the model was appraised with respect to discrimination, calibration ability, and clinical validity. Discrimination was assessed using the AUC, with values > 0.70 indicating relatively good discrimination [24]. DeLong test was used for the comparison between AUC values. The quantities of true positive samples (TP), false positive samples (FP), true negative samples (TN), and false negative samples (FN) were utilized to construct the confusion matrix, from which recall, accuracy, precision, and F_1-score were subsequently calculated, the calculation formula is as follows. In constructing the confusion matrix for the model, we chose a threshold of 0.5. The rationale for this selection is as follows: first, a threshold of 0.5 provides a balanced approach for probability

predictions, where a probability greater than 0.5 indicates a higher likelihood of disease, and a probability below 0.5 suggests a lower likelihood. Second, in the absence of additional prior information or specific requirements, a threshold of 0.5 offers an equitable balance between sensitivity and specificity. Finally, this threshold is commonly used in binary classification problems, facilitating the evaluation of model performance and subsequent fine-tuning. The extent of concordance between the forecasted probabilities and the actual results was evaluated using calibration curves [25]. Discrimination and calibration were both evaluated using bootstrapping with 1000 resamples. The clinical validity was examined utilizing the DCA [26].The potential of multicollinearity among the covariates is assessed by the Variance Inflation Factor (VIF), with a VIF value greater than 3 indicating considerable collinearity [27]. Five sensitivity analyses were performed to assess how the prediction model varied under different conditions. The first analysis excluded individuals aged 60 years and older. The second analysis excluded males. The third analysis employed the mean imputation method to address missing values. The fourth analysis examined the interaction between TyG and other variables. Finally, the fifth analysis tested random forest (RF) as an alternative selection method.

$$\text{Recall} = \frac{\text{TP}}{\text{TP} + \text{FN}}$$

$$\text{Accuracy} = \frac{\text{TP} + \text{TN}}{\text{TP} + \text{TN} + \text{FP} + \text{FN}}$$

$$\text{Precision} = \frac{\text{TP}}{\text{TP} + \text{FP}}$$

$$\text{F}_1 - \text{score} = \frac{2*\text{Recall}*\text{Precision}}{\text{Recall} + \text{Precision}}$$

Statistical analysis

In analyzing continuous variables that adhere to a normal distribution, results were represented using the mean ± standard deviation (SD). Concurrently, an independent two-sample Student's t-test was applied to compare variables across different groups. In cases where continuous variables demonstrated non-normal distribution characteristics, the data were delineated by medians and interquartile ranges (*P*25, *P*75). Subsequently, the Mann-Whitney U test was deployed to statistically evaluate group disparities. Frequencies and their corresponding percentages were used to represent categorical data, and intergroup comparisons were predominantly conducted using the chi-square test, Fisher's exact probability method for analyses involving small sample sizes, or where the assumptions of the chi-square test were not met.

The present research's statistical analysis was executed using the statistical tool R (version 4.4.0) and the Statistical Package for Social Sciences (SPSS) version26.0 software (IBM Corporation, Armonk, NY, USA). The criterion for statistical meaningfulness was defined as a *P* value threshold below 0.05.

Results

Participant baseline characteristics

The study involved 1501 patients presenting with chest pain who underwent CAG. Table 1 provides a detailed summary of the baseline characteristics of these patients, including their demographic information and clinical and laboratory data. Participants were stratified into two groups based on the findings from the CAG: CHD ($n = 1169$) and non-CHD ($n = 332$) groups. Among the patients in the CHD group, 747 cases of angina pectoris, 388 cases of myocardial infarction, and 34 cases of subclinical CHD accounted for 63.90%, 33.20%, and 2.90%, respectively. Among the participants were 865 males (57.60%) and 636 females (42.40%), with a mean age of 60.45 ± 9.32 years. Individuals diagnosed with CHD were older compared to their non-CHD counterparts (60.95 ± 9.39 vs. 58.68 ± 8.82 years). The CHD group exhibited higher prevalence rates of male gender, smoking, hypertension, diabetes, history of stroke, RWMA, and ST-T changes. Notable increases were observed in TyG (9.01 ± 0.70 vs. 8.85 ± 0.55), MHR [0.34 (0.25, 0.47) vs. 0.29 (0.22, 0.41)], as well as in SBP, white blood cell count (WBC), hemoglobin (Hb), FPG, fibrinogen degradation products (FDP) and PTP within the CHD group. At the same time, the levels of HDL-C exhibited a notable decrease ($P < 0.05$). No meaningful differences in the included factors are presented in Table 2 between the training and validation cohorts, with all *P* values exceeding 0.05.

Potential predictors associated with CHD

Initially, the univariate logistic regression analysis incorporated potential risk factors, with those displaying statistical significance (*P* value < 0.05) subsequently assessed in the multivariate logistic regression. In the training set, the TyG exhibited an odds ratio (OR) of 1.56 (95% CI: 1.25–1.96), achieving statistical significance at $P < 0.001$. Concurrently, the MHR index revealed an OR of 6.88 (95% CI: 2.72–17.93) and achieved statistical significance with a $P < 0.001$. In addition, male, age, hypertension, diabetes, smoking, hyperlipidemia, SBP, RWMA, ST-T changes, FDP, and LDL-C were all found to exhibit notable correlations with CHD.

In the following multivariate regression analysis employing the backward stepwise approach, independent

Table 1 Baseline characteristics of the study population

Variable	Total (*n* = 1501)	CHD (*n* = 1169)	Non-CHD (*n* = 332)	t/χ^2/Z	*P* Value
Gender (%)				37.474	< 0.001
Male	865 (57.60)	721 (61.70)	144 (43.40)		
Female	636 (42.40)	448 (38.30)	188 (56.60)		
Chest pain type (%)				63.691	< 0.001
Typical angina	534 (35.60)	455 (38.90)	79 (23.80)		
Atypical angina	637 (42.40)	508 (43.50)	129 (38.90)		
Nonanginal chest pain	330 (22.00)	206 (17.60)	124 (37.30)		
Age (years)	60.45 ± 9.32	60.95 ± 9.39	58.68 ± 8.82	-3.927	< 0.001
BMI (kg/m^2)	25.57 ± 3.44	25.56 ± 3.47	25.61 ± 3.35	0.250	0.803
Heart rate (beats/min)	76.47 ± 12.93	76.33 ± 13.11	76.96 ± 12.37	0.788	0.431
SBP (mmHg)	136.96 ± 20.56	137.69 ± 20.97	134.39 ± 18.82	-2.747	0.006
DBP (mmHg)	82.57 ± 12.76	82.56 ± 13.11	82.61 ± 11.45	0.075	0.940
Smoking (%)	686 (45.70)	576 (49.30)	110 (33.10)	27.144	< 0.001
Drinking (%)	493 (32.80)	398 (34.00)	95 (28.60)	3.459	0.063
Previous history					
Hypertension (%)	934 (62.20)	761 (65.10)	173 (52.10)	18.562	< 0.001
Diabetes (%)	429 (28.60)	367 (31.40)	62 (18.70)	20.494	< 0.001
Hyperlipidemia (%)	907 (60.40)	726 (62.10)	181 (54.50)	6.223	0.013
Hyperuricemia (%)	270(18.30)	204 (17.70)	66 (20.40)	1.687	0.446
Stroke (%)	288 (19.20)	241 (16.10)	47 (14.20)	6.957	0.008
Family history of CHD (%)	152 (10.10)	123 (10.50)	29 (8.70)	0.907	0.341
Family history of diabetes (%)	58 (3.90)	47 (4.00)	11 (3.30)	0.348	0.555
Laboratory test index					
WBC (×10^9/L)	6.20 (5.20, 7.50)	6.30(5.30, 7.70)	5.90(4.95, 7.15)	-4.400	< 0.001
RBC (×10^{12}/L)	4.56 ± 0.54	4.57 ± 0.55	4.53 ± 0.51	-1.065	0.287
Hb (g/L)	141.62 ± 15.34	142.10 ± 15.56	139.91 ± 14.43	-2.300	0.022
RDW	14.00 (13.20, 14.65)	13.90 (13.20, 14.60)	14.00 (13.30, 14.70)	-1.284	0.199
PLT (×10^9/L)	210.00 (177.00,247.00)	209.00(177.00, 245.00)	211.00 (179.50, 248.50)	-0.579	0.563
Mono (×10^9/L)	0.36 (0.28, 0.47)	0.37 (0.28, 0.48)	0.35 (0.27, 0.44)	-2.638	0.080
MHR	0.33 (0.38, 0.45)	0.34 (0.25, 0.47)	0.29 (0.22, 0.41)	-4.800	< 0.001
DD (ng/mL)	89.00 (57.00, 133.00)	91.00 (58.00, 136.00)	81.00 (56.00, 124.74)	-1.812	0.070
FDP (ug/mL)	0.78 (0.43, 1.24)	0.80 (0.46, 1.30)	0.69 (0.31, 1.10)	-3.515	< 0.001
FPG (mmol/L)	5.50 (5.00, 6.60)	5.60 (5.00, 6.90)	5.30 (4.90, 6.00)	-4.244	< 0.001
TG (mmol/L)	1.57 (1.12, 2.30)	1.59 (1.12, 2.39)	1.52 (1.12, 2.07)	-1.934	0.053
TC (mmol/L)	4.28 ± 1.06	4.30 ± 1.08	4.22 ± 0.99	-1.146	0.252
HDL-C (mmol/L)	1.08 (0.93, 1.28)	1.07 (0.92, 1.25)	1.17 (1.00, 1.36)	-5.475	< 0.001
LDL-C (mmol/L)	2.25 (1.73,2.78)	2.28 (1.75, 2.79)	2.20 (1.68, 2.73)	-1.599	0.110
TyG	8.97 ± 0.67	9.01 ± 0.70	8.85 ± 0.55	-4.535	< 0.001
RWMA (%)	871 (58.00)	715 (61.20)	156 (47.00)	21.333	< 0.001
ST-T changes (%)	778 (51.80)	667 (57.10)	111 (33.40)	57.797	< 0.001
PTP	0.45 ± 0.22	0.48 ± 0.21	0.35 ± 0.19	-10.87	< 0.001

Abbreviations: CHD, Coronary heart disease; BMI, Body mass index; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; WBC, White blood cell count; RBC, Red blood cell count; Hb, Hemoglobin; RDW, Red blood cell distribution width; PLT, Platelet count; Mono, Monocyte count; MHR, Monocyte-to-high-density lipoprotein cholesterol ratio; DD, D-dimer; FDP, Fibrinogen degradation products; FPG, Fasting plasma glucose; TG, Triglyceride; TC, Total cholesterol; HDL-C, High-density lipoprotein cholesterol; LDL-C, Low-density lipoprotein cholesterol; TyG, Triglyceride-glucose index; RWMA, Regional wall motion abnormality; PTP, Pretest probability

Fisher's exact test

predictors for CHD were identified. The TyG was a significant predictor ($P = 0.043$), with an OR of 1.34 (95% CI: 1.01–1.77). The MHR ($P = 0.020$) was also identified with an OR of 3.07 (95% CI: 1.19–7.91), indicating its association with CHD. Other conventional predictors included male, age, SBP, RWMA, and ST-T changes. A forest plot based on these results was generated to represent the strength and direction of these associations visually, and the detailed consequences are provided in Table 3 and graphically described in Fig. 2.

Table 2 Baseline characteristics of training and validation set

Variable	Training set (*n* = 1051)	Validation set (*n* = 450)	t/χ^2/Z	*P* Value
CHD (%)	818 (77.80)	351 (78.00)	0.005	0.942
Gender (%)			0.144	0.704
Male	609 (57.90)	256 (56.90)		
Female	442 (42.10)	194 (43.10)		
Chest pain type (%)			1.329	0.515
Typical angina	369 (35.10)	165 (36.70)		
Atypical angina	456 (43.40)	181 (40.20)		
Nonanginal chest pain	226 (21.50)	104 (23.10)		
Age (years)	60.35 ± 9.35	60.67 ± 9.25	-0.598	0.550
BMI (kg/m^2)	25.49 ± 3.40	25.75 ± 3.55	-1.344	0.179
Heart rate (beats/min)	76.93 ± 12.72	76.15 ± 13.41	1.067	0.286
SBP (mmHg)	137.31 ± 20.67	136.15 ± 20.29	1.003	0.316
DBP (mmHg)	82.84 ± 12.53	81.94 ± 13.27	1.244	0.214
Smoking (%)	483 (46.00)	203 (45.10)	0.091	0.763
Drinking (%)	349 (33.20)	144 (32.00)	0.208	0.648
Previous history				
Hypertension (%)	667 (63.50)	267 (59.30)	2.287	0.131
Diabetes (%)	313 (29.80)	116 (25.80)	2.474	0.116
Hyperlipidemia (%)	628 (59.80)	279 (62.00)	0.666	0.415
Hyperuricemia (%)	186 (17.70)	87 (19.30)	0.567	0.452
Stroke (%)	200 (19.00)	88 (19.60)	0.056	0.813
Family history of CHD (%)	112 (10.70)	40 (8.90)	1.082	0.298
Family history of diabetes (%)	45 (4.30)	13 (2.90)	1.645	0.200
Laboratory test index				
WBC (×10^9/L)	6.20 (5.25, 7.50)	6.20 (5.20, 7.50)	-1.723	0.085
RBC (×10^{12}/L)	4.58 ± 0.52	4.54 ± 0.59	1.271	0.204
Hb (g/L)	141.72 ± 15.22	141.39 ± 15.63	0.381	0.703
RDW	13.90 (13.20, 14.60)	14.00 (13.30, 14.70)	-1.856	0.063
PLT (×10^9/L)	208.00 (177.00,244.00)	213.00 (178.00, 250.00)	-0.210	0.834
Mono (×10^9/L)	0.36 (0.28, 0.47)	0.35 (0.28, 0.46)	-0.509	0.611
MHR	0.33 (0.23, 0.45)	0.33 (0.24, 0.45)	-0.372	0.710
DD (ng/mL)	87.00 (56.11, 129.00)	97.50 (59.00, 141.00)	-0.660	0.509
FDP (ug/mL)	0.78 (0.44, 1.23)	0.78 (0.42, 1.25)	-0.247	0.805
FPG (mmol/L)	5.50 (4.90, 6.70)	5.50 (4.90, 6.40)	-0.044	0.965
TG (mmol/L)	1.56 (1.13, 2.28)	1.59 (1.11, 2.34)	-1.550	0.121
TC (mmol/L)	4.28 ± 1.07	4.28 ± 1.04	-0.063	0.950
HDL-C (mmol/L)	1.09 (0.93, 1.30)	1.08 (0.91, 1.26)	-0.441	0.659
LDL-C (mmol/L)	2.25 (1.74, 2.78)	2.28 (1.73, 2.76)	-1.510	0.131
TyG	9.01 ± 0.70	8.85 ± 0.55	-0.117	0.907
RWMA (%)	613 (58.30)	258 (57.30)	0.127	0.721
ST-T changes (%)	534 (50.80)	244 (54.20)	1.471	0.225
PTP	0.45 ± 0.22	0.45 ± 0.21	0.147	0.883

Abbreviations: CHD, Coronary heart disease; BMI, Body mass index; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; WBC, White blood cell count; RBC, Red blood cell count; Hb, Hemoglobin; RDW, Red blood cell distribution width; PLT, Platelet count; Mono, Monocyte count; MHR, Monocyte-to-high-density lipoprotein cholesterol ratio; DD, D-dimer; FDP, Fibrinogen degradation products; FPG, Fasting plasma glucose; TG, Triglyceride; TC, Total cholesterol; HDL-C, High-density lipoprotein cholesterol; LDL-C, Low-density lipoprotein cholesterol; TyG, Triglyceride-glucose index; RWMA, Regional wall motion abnormality; PTP, Pretest probability

Predictive model development

A multivariate logistic regression established a predictive model. The VIF test showed VIF values < 2 for all variables, indicating no multicollinearity and confirming good model fit. The prediction model included the following statistically significant variables: TyG, MHR, male, age, diabetes, SBP, RWMA, ST-T changes, and LDL-C. A nomogram graphically represented the predictive model, providing a tool for quantifying CHD risk in chest pain patients (Fig. 3).

Table 3 Univariate and multivariate logistic regression analysis of risk factors for CHD

Variable	Univariate analysis			Multivariate analysis		
	OR	95% CI	*P* Value	OR	95% CI	*P* Value
Male	2.14	1.59–2.88	< 0.001	2.60	1.86–3.62	< 0.001
Age	1.03	1.01–1.04	< 0.001	1.05	1.03–1.07	< 0.001
BMI	0.98	0.94–1.03	0.428	-	-	-
Hypertension	1.59	1.18–2.13	0.002	-	-	-
Diabetes	1.79	1.26–2.53	0.001	1.47	0.99–2.18	0.055
Stroke	1.27	0.86–1.88	0.231	-	-	-
Smoking	1.86	1.37–2.52	< 0.001	-	-	-
Drinking	1.27	0.93–1.74	0.140	-	-	-
Hyperlipidemia	1.41	1.05–1.89	0.021	-	-	-
Hyperuricemia	0.87	0.60–1.26	0.464	-	-	-
Family history of CHD	1.35	0.81–1.35	0.247	-	-	-
Family history of diabetes	1.15	0.54–2.41	0.720	-	-	-
Heart rate	0.95	0.90–1.01	0.343	-	-	-
SBP	1.01	1.00-1.02	0.008	1.01	1.00-1.02	0.046
DBP	1.00	0.99–1.02	0.470	-	-	-
RWMA	1.71	1.27–2.29	< 0.001	1.45	1.06–1.99	0.020
ST-T changes	2.50	1.85–3.40	< 0.001	2.16	1.56–2.98	< 0.001
TyG	1.56	1.25–1.96	< 0.001	1.34	1.01–1.77	0.043
MHR	6.88	2.72–17.39	< 0.001	3.07	1.19–7.91	0.020
DD	1.00	1.00-1.03	0.057	-	-	-
FDP	1.15	1.02–1.29	0.024	-	-	-
TC	1.14	0.99–1.31	0.071	-	-	-
LDL-C	1.28	1.06–1.55	0.010	1.25	1.01–1.54	0.039

Abbreviations: OR, Odds ratio; CI, Confidence interval; BMI, Body mass index; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; TyG, Triglyceride-glucose index; MHR, Monocyte-to-high-density lipoprotein cholesterol ratio; DD, D-dimer; FDP, Fibrinogen degradation products; TC, Total cholesterol; LDL-C, Low-density lipoprotein cholesterol; RWMA, Regional wall motion abnormality

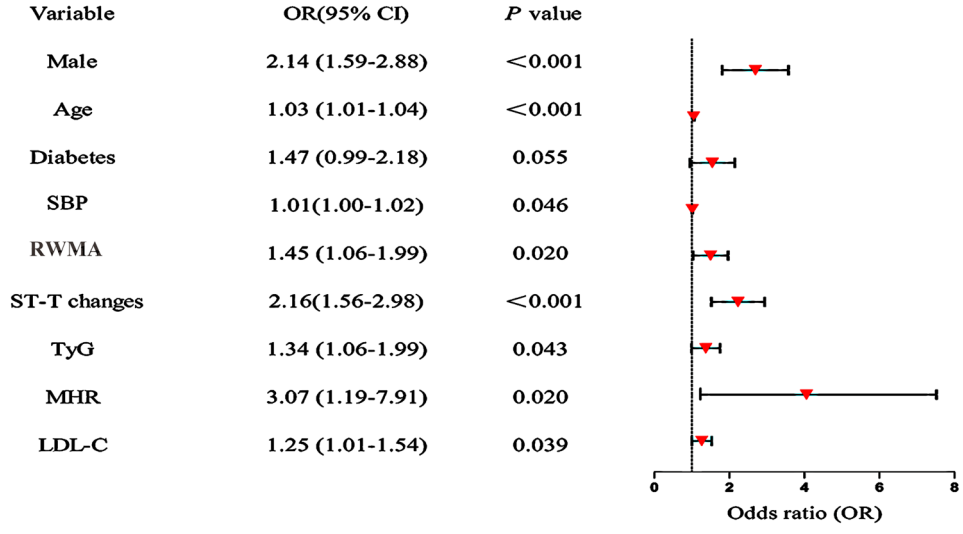

Fig. 2 Forest plot for multivariate regression analysis of the training set. Abbreviations: OR, Odds ratio; CI, Confidence interval; SBP, Systolic blood pressure; TyG, Triglyceride-glucose; MHR, Monocyte-to-high-density lipoprotein cholesterol ratio; LDL-C, Low-density lipoprotein cholesterol; RWMA, Regional wall motion abnormality

Predictive model validation

Confusion matrices

The confusion matrices for the training and validation set are presented in Fig. 4. The sum of TP and TN samples indicates the number of correct predictions by the model. In the training set, there were 560 TP and 154 TN samples (Fig. 4A), while the validation set included 274 TP and 57 TN samples (Fig. 4B). In the training set, the recall was 0.685, accuracy was 0.679, precision was 0.876, and the F_1-score was 0.769. The validation set exhibited a

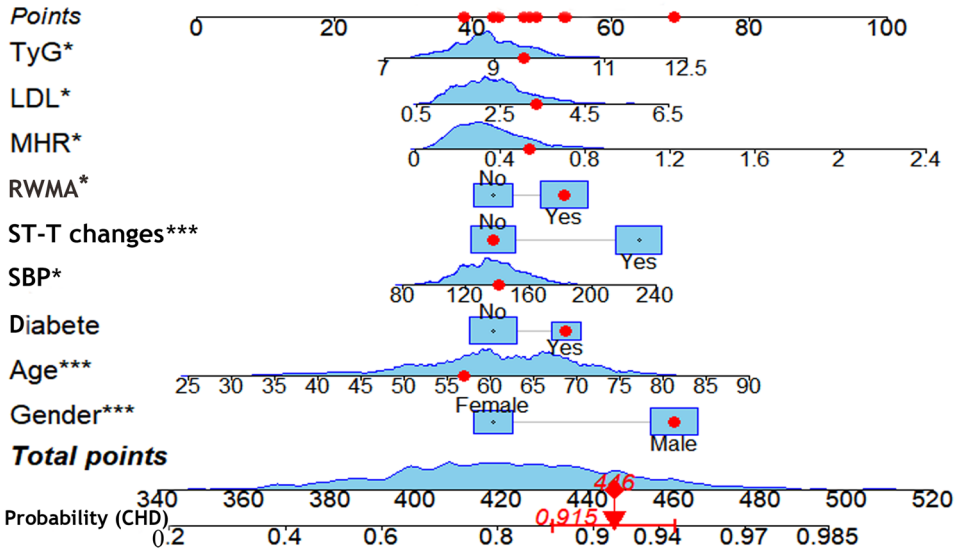

Fig. 3 Nomogram of training set. Abbreviations: SBP, Systolic blood pressure; MHR, Monocyte-to-high-density lipoprotein cholesterol ratio; LDL-C, Low-density lipoprotein cholesterol; TyG, Triglyceride-glucose; CHD, Coronary heart disease; RWMA, Regional wall motion abnormality

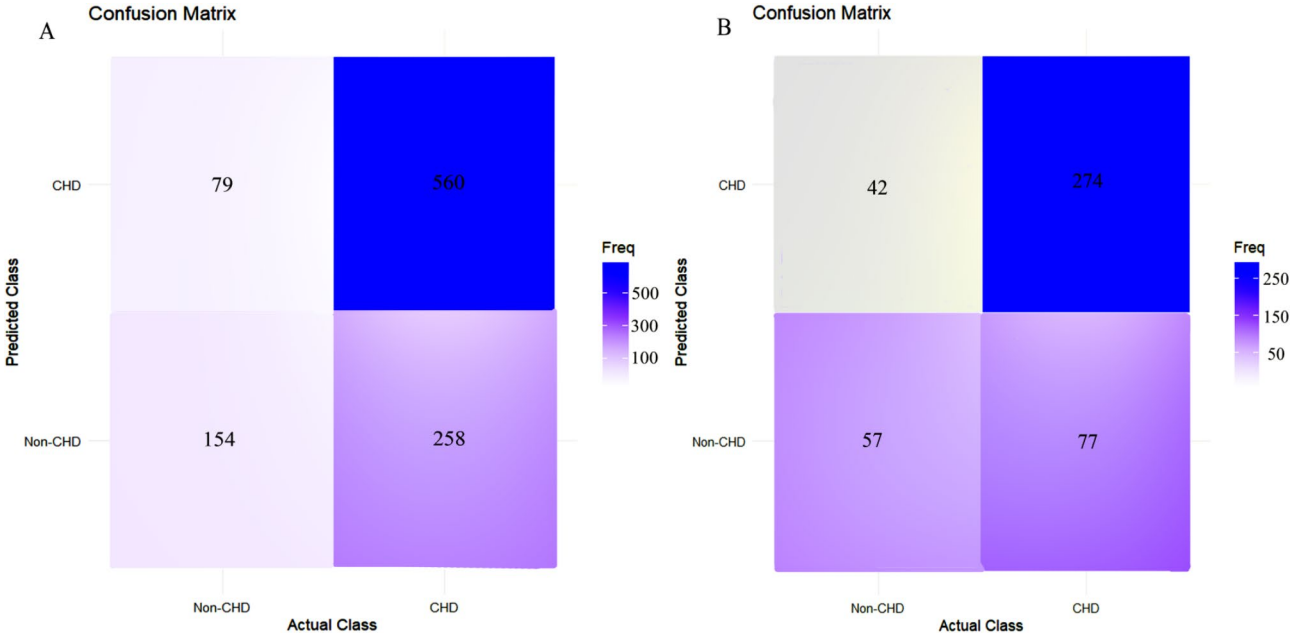

Fig. 4 Confusion Matrix of the training set and validation set; **A** Confusion Matrix of the training set; **B** Confusion Matrix of the validation set

Table 4 Forecast results for training and validation set

Indicator	Training set	Validation set
Recall	0.685	0.781
Accuracy	0.679	0.736
Precision	0.876	0.867
F_1-score	0.769	0.822

recall of 0.781, accuracy of 0.736, precision of 0.867, and an F_1-score of 0.822 (Table 4).

Discrimination of the predictive model

The model exhibits a substantial degree of discrimination, as depicted in Fig. 5. The training set resulted in an AUC was calculated to be 0.733 (95% CI: 0.698–0.768), and the specificity and sensitivity were recorded as 66.1% and 68.5%, respectively. The validation set exhibited similar performance, with an AUC of 0.721 (95% CI: 0.663–0.779), specificity at 57.6% and sensitivity at 78.1%. At the

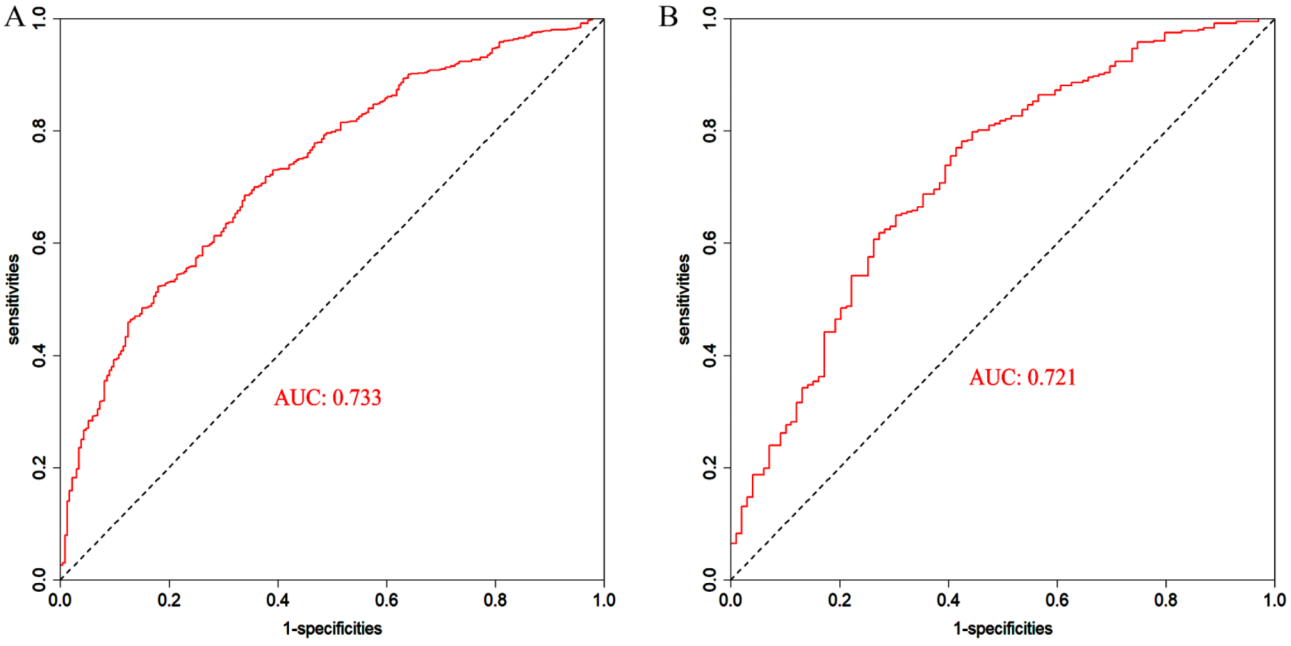

Fig. 5 ROC curves for the training set and validation set; **A** ROC curves for the training set; **B** ROC curves for the validation set. Abbreviations: AUC, Area under the receiver operating characteristic curve

sum of sensitivity and specificity reaches its maximum, corresponding to the point at which the Youden index attains its maximum value, the sensitivity and specificity were 76.6% and 58.6%, respectively; in addition, at the sensitivity is set at a specific value of 80.0%, the sensitivity and specificity were 80.0%and 50.1%, respectively. The specificity of the latter is lower than that of both the training set and the validation set.

Calibration of the predictive model

When appraising the goodness of fit for the nomogram, the calibration curves revealed a strong concordance between estimated probabilities and the observed incidence of CHD, indicating a reliable model fit. The Hosmer-Lemeshow goodness-of-fit test outcomes were delineated as $\chi2 = 6.639$ ($P = 0.576$) for the training set and $\chi2 = 5.581$ ($P = 0.694$) for the validation set, both with P value exceeding 0.05, suggesting the model fit excellent (Fig. 6).

Evaluation of clinical validity

To determine the practical applicability of the risk-stratification model in clinical settings, DCA was performed, and the findings are graphically represented in Fig. 7. The DCA curves indicated that the nomogram would be beneficial for predicting CHD within a threshold probability range of 0.11–0.73 in the training set and 0.09–0.67 in the validation set.

Sensitivity analysis

In analyses that excluded individuals aged 60 years and older, the AUC of the model was 0.719 (95%CI: 0.674–0.763), which was comparable to the results of the primary model. Similarly, in the analysis excluding the male population, the AUC was 0.721 (95% CI: 0.679–0.763), again showing results consistent with the primary model. Missing data represented less than 6% of the key variables in this study. To address the missing values, we applied the mean imputation method, which resulted in an AUC of 0.726 (95% CI: 0.696–0.756). Further stratified analyses were conducted to explore potential interaction effects. The results indicated that the main effect remained consistent across different subgroups, with similar effect sizes and directions. Importantly, no significant interactions were observed (P for interaction > 0.05), suggesting that the model's results are robust and stable (Supplemental Fig. 1S). Additionally, the use of the Random Forest (RF) method did not improve the AUC (0.632, 95% CI: 0.592–0.672) when compared to the logistic regression model.

Comparison between models

The comparison between the constructed model and the guide-recommended PTP revealed that the AUC of the proposed model was significantly higher than that of the PTP (0.721 vs. 0.671), but the difference was not statistically significant (DeLong test: Z = -1.427, $P = 0.154$). Additionally, both sensitivity and accuracy were superior in the proposed model compared to the PTP tool. However, when combining the proposed model and PTP,

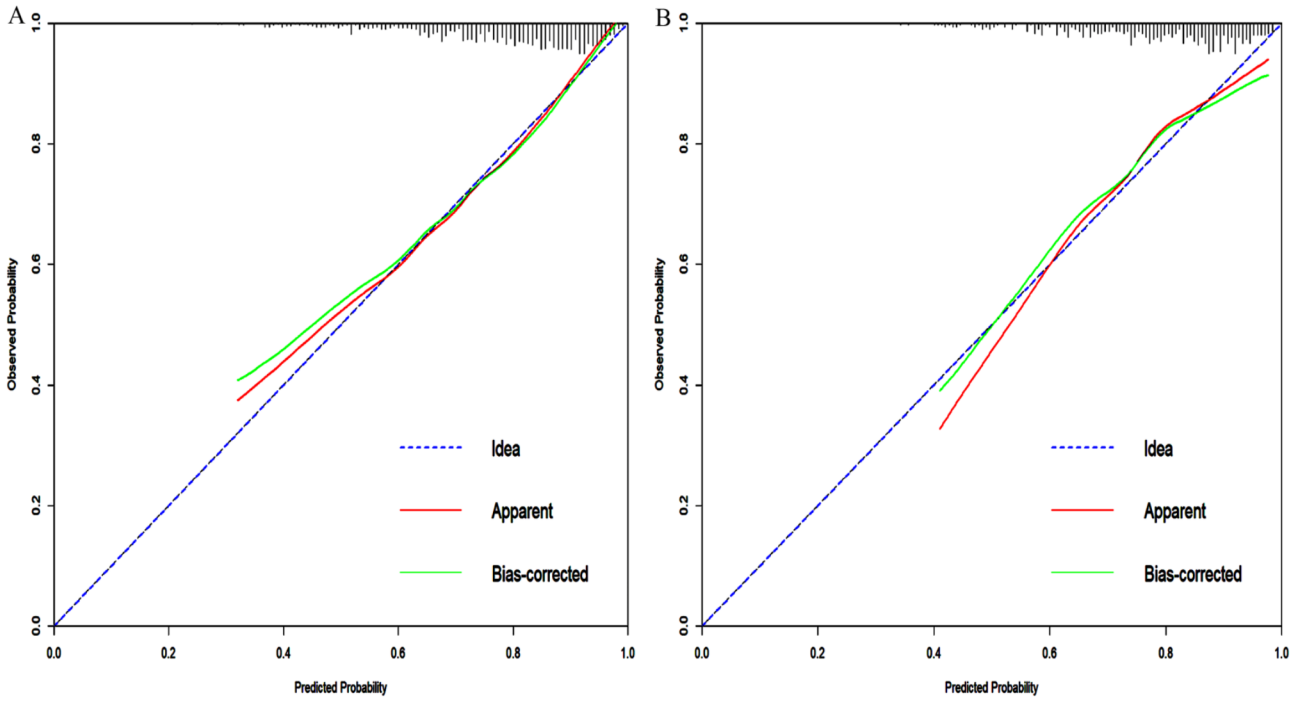

Fig. 6 Calibration plot for the training set and validation set; **A** Calibration plot for the training set; **B** Calibration plot for the validation set

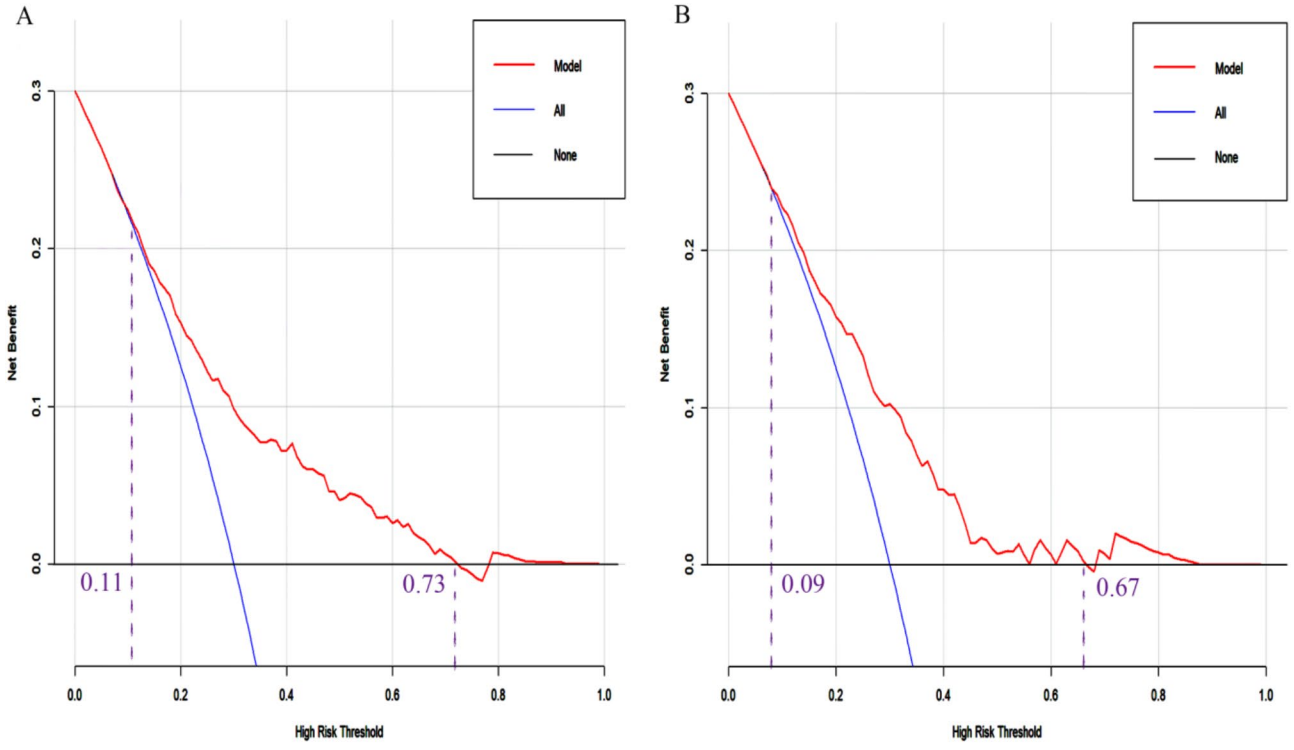

Fig. 7 DCA curves for the training set and validation set; **A** DCA curves for the training set; **B** DCA curves for the validation set

while there was a slight improvement in AUC and specificity, the sensitivity and accuracy showed a decline. The difference between the AUCs of the proposed model combined with PTP and PTP was statistically significant (DeLong test: Z = -3.103, P = 0.002), but the difference between the AUCs of the proposed model combined with PTP and proposed model was not statistically significant (DeLong test: Z = -1.902, P = 0.057). As shown in

Table 5 A comparative analysis between the proposed model and PTP

Index	Estimate	95% CI
AUC		
Proposed model	0.721	0.663–0.779
PTP	0.671	0.614–0.729
Proposed model + PTP	0.749	0.695–0.802
Sensitivity		
Proposed model	0.781	-
PTP	0.510	-
Proposed model + PTP	0.741	-
Specificity		
Proposed model	0.576	-
PTP	0.789	-
Proposed model + PTP	0.657	-
Accuracy		
Proposed model	0.736	-
PTP	0.571	-
Proposed model + PTP	0.722	-
NRI		
Proposed model vs. PTP	20.75	6.28–35.23
Proposed model vs. Proposed model + PTP	32.98	20.05–45.91
IDI		
Proposed model vs. PTP	4.48	2.47–6.49
Proposed model vs. Proposed model + PTP	3.07	1.93–4.21

Abbreviations: CI, Confidence interval; AUC, Area under the curve; PTP: Pretest probability; NRI: Net reclassification improvement; IDI: Integrated discrimination improvement

Table 5, the proposed model improved risk reclassification for CHD compared with PTP, with a net reclassification improvement (NRI) of 20.75% ($P = 0.004$) and an integrated discrimination improvement (IDI) of 4.48% ($P < 0.001$).

Discussion

CHD, which shows a significant rise in incidence with advancing age, has become a prominent public health question both in China and worldwide, representing a considerable risk to human health and well-being [28]. Consequently, this research investigated elements beyond conventional risk factors to identify practical, easily measurable, dependable, and innovative biological markers and develop predictive models for the prompt detection of CHD. This cross-sectional study investigated the correlations between TyG, MHR, and CHD in patients presenting with chest pain. Our research findings suggest that the TyG index and MHR are independent risk factors for CHD. To identify contributory risk factors for CHD among individuals experiencing chest pain, we meticulously conducted univariate logistic regression analysis on the designated training cohort. Subsequently, covariates demonstrating statistical significance ($P < 0.05$) from the univariable logistic regression were advanced to a backward stepwise multivariate logistic regression to ascertain significant predictors for the nomogram. Ultimately, the logistic regression analysis identified nine indicators as predictors, and a prediction model was constructed using the TyG index, MHR, male, age, diabetes, SBP, RWMA, ST-T changes, and LDL-C as predictors.

The development of CHD is intricate and characterized by persistent inflammation and irregular lipid metabolism [29, 30]. This study has recognized TyG as a predictor of CHD in individuals experiencing chest pain, which is consistent with earlier studies [31–34]. Research has found that elevated TyG levels are independently and significantly linked to a heightened risk of CHD, affirming its potential as a dependable and promising indicator of IR [35, 36]. IR triggers an inflammatory response and interferes with insulin signaling in intimal cells, resulting in endothelial dysfunction and vascular remodeling. Additionally, it promotes thrombogenesis by enhancing platelet activation and aggregation, ultimately contributing to the onset of cardiovascular disease [37–39]. Furthermore, IR promotes the differentiation of macrophages into foam cells, thereby contributing to the formation of vulnerable plaques. This process is mediated through the induction of endoplasmic reticulum stress and the activation of macrophage apoptosis pathways. Together, these mechanisms collectively contribute to the necrotic degeneration and potential rupture of atherosclerotic plaques, thereby underscoring the significance of IR in the progression of cardiovascular diseases [40].

Monocytes have been identified as pivotal contributors to the secretion of a spectrum of inflammatory cytokines, which are integral to the pathogenesis of chronic inflammatory states and are significantly implicated in the progression of CHD [41, 42]. HDL-C, primarily produced by the liver and small intestine, provides atheroprotective benefits by promoting reverse cholesterol transport, inhibiting the aggregation, activation, and migration of monocytes, and reducing oxidation of LDL-C [43–45]. Recently, the novel inflammatory marker MHR has emerged as a more precise and comprehensive indicator of vascular inflammation than monocytes and HDL-C alone. Previous research has consistently indicated a significant relationship between MHR and the incidence of CHD, indicating its potential utility as an inflammatory biomarker for diagnosing and predicting CHD [46]. Further investigations have revealed that MHR is significantly linked to the incidence of CHD, as well as its adverse prognosis [9, 47, 48]. The present research results are consistent with previous studies and identify a notable relation between MHR and the incidence of CHD. Consequently, incorporating MHR into the routine evaluation of patients experiencing chest pain can assist clinicians in risk stratification.

Nomograms, commonly utilized predictive models in clinical settings, visually depict the relationships between

variables through connected line segments on a two-dimensional coordinate system. They accurately quantify hazard ratios score form, simplifying patient risk calculations and enhancing accuracy and relevance [49, 50]. Previous research has not developed nomograms for predicting CHD in individuals presenting with chest pain utilizing the TyG and MHR. The innovation of this study consists in constructing an efficient, accurate, and noninvasive predictive model based on TyG and MHR for CHD in patients with chest pain, which assists physicians in screening for CHD and formulating treatment strategies.

In the predictive model, every patient presenting with chest pain was assigned a personalized score derived from the nomogram, which allowed for precise categorization into low and high-risk groups; the details of scoring on the nomogram are detailed in the supplementary material. When the nomogram indicates a high probability of CHD, it is advisable to pursue further CAG to detect patients with underlying CHD, as the advantages of prompt revascularization are well established. This advancement will significantly enhance patient care by minimizing unnecessary invasive procedures and facilitating the initiation of appropriate treatment. We can improve secondary prevention by using non-invasive, low-cost, and easily obtainable indicators that demonstrate high sensitivity and specificity in diagnostic programs for early diagnosis. Moreover, our nomogram model can assist patients presenting with chest pain in assessing their disease risk, enhancing their awareness of CHD risk factors, and consequently improving their adherence to medical recommendations.

Following internal validation, we determined that the nomogram model developed exhibits a significant degree of discriminative ability, evidenced by an AUC of 0.721, and its predictive performance exceeds that of the traditional PTP tool. The model demonstrates commendable goodness of fit and accuracy, along with substantial precision, enabling reliable estimation of the probability of CHD in patients presenting with chest pain. For example, consider a patient with the following characteristics: TyG of 9.55 (score of 48), MHR of 0.54 (score of 49), male (score of 69), age of 57 years (score of 39), a history of diabetes (score of 53), SBP of 141 mmHg (score of 44), presence of wall-motion abnormalities (score of 53 points), no ST-T changes (score of 43 points), LDL-C of 3.35 mmol/L (score of 48 points), and according to the nomogram, the individual scores for these variables can be identified on the corresponding line segments. Summing these scores yields a total score of 446 points, which predicts a risk of CHD of 0.915 for this patient, categorizing them as high risk. Clarifying the influencing factors on the occurrence of CHD in patients presenting chest pain and utilizing a visual nomogram to individually predict the CHD risk conducive healthcare personnel to identify CHD risk more conveniently and effectively and to take targeted measures to intervene as soon as possible, which is essential for improving the recognition rate of patients with chest pain, shortening the length of hospitalization, improving the quality of life, and decreasing the morbidity and mortality rate of CHD. In future research, we will increase the sample size and perform external validation to enhance the model's reliability and generalizability. This study will establish a foundation for the subsequent development of CHD risk prediction software, systems, or applications for patients presenting with chest pain, thereby providing valuable references for clinical medical professionals in identifying high-risk CHD populations among these patients.

Strengths and limitations of the study

Several salient strengths distinguish the current research. First, a systematic approach was undertaken to identify the independent risk factors for CHD. The identification of these risk factors was achieved rigorously by applying univariate and multivariate logistic regression analyses, which adjusted potential confounders' effects. Second, the model offers a precise and quantitative tool for individual CHD risk assessment through its presentation as a nomogram. Furthermore, the predictive model presented in this research demonstrates significant discrimination and calibration, confirming its potential clinical utility. However, there are limitations to consider. Firstly, the nomogram was developed using data from a single center, necessitating further external validation to ensure generalizability. Secondly, the sample size of 1501 subjects was limited. Future research endeavors should prioritize an enlargement of the participant number to verify the reliability of predictive models. Thirdly, while multivariate logistic regression analysis was employed to control for confounding bias, the influence of unmeasured confounders may still affect the result. Fourth, the study population consisted solely of hospitalized patients, which might restrict the generalizability of the findings to outpatient populations. Fifth, the sensitivity of this predictive model is 78.1% greater than its specificity, indicating a significant predictive value for assessing the risk of CHD in patients presenting with chest pain, thereby offering valuable insights for clinicians. However, it cannot be utilized as a definitive criterion for the inclusion or exclusion of CHD at this time; further research and validation are warranted in the future. Sixth, as a cross-sectional study without follow-up, future research should include long-term follow-up data to comprehensively evaluate the nomogram's efficacy and the causal relationships among the variables. Finally, our study focused exclusively on patients who underwent CAG testing rather than all individuals with suspected CHD, which

may introduce information bias. Furthermore, this study used a coronary artery stenosis of ≥ 50% as the diagnostic criterion for CHD, without considering coronary blood flow status. This approach, which is based solely on the severity of anatomical stenosis, may not fully capture the true extent of myocardial ischemia. Future studies should, if feasible, incorporate fractional flow reserve (FFR) to provide a more comprehensive assessment in the diagnosis of CHD.

Conclusion

The nomogram incorporating TyG, MHR, and conventional risk factors (gender, age, diabetes, RWMA, ST-T changes, and LDL-C) was internally verified. This model exhibited good discriminative ability, calibration, and a favorable net benefit. Its predictive performance exceeds that of the traditional PTP tool and may serve as a non-invasive and promising approach to aid clinicians in the early identification of CHD risk in patients presenting with chest pain. However, the nomogram was developed using data from a single center, necessitating further external validation to ensure generalizability.

Abbreviations

CHD	Coronary heart disease
TyG	Triglyceride-glucose
MHR	Monocyte-to-high-density lipoprotein cholesterol ratio
BMI	Body mass index
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
WBC	White blood cell count
RBC	Red blood cell count
Hb	Hemoglobin
RDW	Red blood cell distribution width
PLT	Platelet count
Mono	Monocyte count
DD	D-dimer
FDP	Fibrinogen degradation products
FPG	Fasting plasma glucose
TG	Triglyceride
TC	Total cholesterol
HDL-C	High-density lipoprotein cholesterol
LDL-C	Low-density lipoprotein cholesterol
RWMA	Regional wall motion abnormality
PTP	Pretest probability
OR	Odds ratio
CI	Confidence interval
AUC	Area under the receiver operating characteristic curve
NRI	Net reclassification improvement
IDI	Integrated discrimination improvement

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12944-025-02486-w .

Supplementary Material 1

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Author contributions

Each author contributed to this research work in various ways. The contributions of each author are outlined below: DL designed the study. HY, JD, RG, MS, JG, HJS, HS, XZ, YS, and YH contributed to the collection and management of the data. HY, JD, RG, MS, JG and DL performed data analysis and drafted the manuscript. DL and XW reviewed and revised the manuscript. All authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This cross-sectional study conformed to the Declaration of Helsinki and was approved by the Ethics Committee of Chengde Central Hospital. Written informed consent was obtained from all the patients.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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