Original article

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Validation of a predictive model for coronary artery disease in patients with diabetes

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Background **No reliable model can currently be used for predicting coronary artery disease (CAD) occurrence in patients with diabetes. We developed and validated a model predicting the occurrence of CAD in these patients.**

Methods **We retrospectively enrolled patients with diabetes at Henan Provincial People's Hospital between 1 January 2020 and 10 June 2020, and collected data including demographics, physical examination results, laboratory test results, and diagnostic information from their medical records. The training set included patients ($n = 1152$) enrolled before 15 May 2020, and the validation set included the remaining patients ($n = 238$). Univariate and multivariate logistic regression analyses were performed in the training set to develop a predictive model, which were visualized using a nomogram. The model's performance was assessed by area under the receiver-operating characteristic curve (AUC) and Brier scores for both data sets.**

Results **Sex, diabetes duration, low-density lipoprotein, creatinine, high-density lipoprotein, hypertension, and heart rate were CAD predictors in diabetes patients. The model's AUC and Brier score were 0.753 [95% confidence interval (CI) 0.727–0.778] and 0.152, respectively, and 0.738 (95% CI 0.678–0.793) and 0.172, respectively, in the training and validation sets, respectively.**

Conclusions **Our model demonstrated favourable performance; thus, it can effectively predict CAD occurrence in diabetes patients.**

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Keywords: creatinine, high-density lipoproteins, hypertension, low-density lipoproteins, nomogram

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Introduction

Coronary artery disease (CAD) is caused by stenosis and/or obstruction in the coronary vessels, which results in the deprivation of oxygen and nutrients to the cardiac muscle. CAD is categorized as stable angina, unstable angina, myocardial infarction, or coronary death based on the clinical presentation.[1] It represents the third major disease burden worldwide, accounting for 6.8% and 5.3% of disability-adjusted life years lost in male and female adults, respectively. It caused 8.93 million deaths in 2017, accounting for approximately 16.0% of global deaths,[2] and is projected to remain the leading cause of death worldwide until 2030.[3]

Diabetes mellitus (DM), a rapidly progressing endocrinal disease, affected nearly 415 million adults worldwide in 2015,[4] and is set to reach 693 million by 2045.[5] Its diagnosis is characterized by a high level of blood glucose, and it is usually accompanied by several complications, such as diabetic kidney disease and diabetic retinopathy, which impose a huge burden on society and patients' families.[6,7] Cardiovascular disease, one of its devastating complications, leads to increased morbidity and mortality in people living with diabetes (PLWD),[8] with PLWD having a two- to fourfold greater risk of developing CAD than those without diabetes.[9] Although risk factors related to CAD were identified in patients with type 2 diabetes in randomized clinical trials,[10] no reliable model for predicting the occurrence of CAD in patients with diabetes has been developed. Therefore, this study aimed to develop a predictive model for detecting patients with a high risk of CAD based on demographics, habits, and laboratory parameters to provide appropriate care.

Methods

Considering that there might be 15 variables in the final model, with an incidence rate of 20% for CAD in DM patients and a predicted 20% dropout rate, we intended to recruit 750 participants in our study.[11] We consecutively included patients admitted to the hospital because of a diagnosis of diabetes between 1 January 2020 and 15 May 2020. The inclusion criteria were as follows: DM

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diagnosis by a clinician according to the guidelines for prevention and treatment of diabetes in China, and participant age ≥18 years, patients diagnosed with or without previous CAD. Patients diagnosed with gestational DM or those with considerably missing data (>30% of the variables) were excluded. Furthermore, data for PLWD, who met the inclusion criteria, were sampled consecutively between 16 May 2020 and 10 June 2020, and served as the validation set.

We retrieved clinical data of the patients that were recorded on their first admission from their medical records. The relevant data included: demographics and physical examination results, including age, sex, weight, height, body mass index, blood pressure, smoking and drinking habits, diabetes duration, pulse, respiratory rate; laboratory test parameters including: white blood cell count (WCC), red blood cell count (RBC), blood platelet count, haemoglobin (HB), C-reactive protein (CRP), alanine transaminase (ALT), aspartate aminotransferase (AST), serum albumin, globulin, total bilirubin, direct bilirubin, indirect bilirubin, serum total bile acid, alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), creatine kinase, creatine kinase myocardial band, lactate dehydrogenase, ischemia-modified albumin, total cholesterol (TC), triglycerides, high-density lipoprotein (HDL), low-density lipoprotein (LDL), apolipoprotein A1 (APOA1), apolipoprotein B100 (APOB100), CO_2, blood urea, creatinine (CREA), urinalysis, retinol-binding protein (RbP), fibrinogen, cystatin C (CYC), glycated haemoglobin, prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin time, thrombin time, free triiodothyronine (FT3), free thyroxine (FT), and thyroid-stimulating hormone (TSH); and diagnostic information concerning CAD, that is, International Classification of Disease-9 Codes, diagnosed by some noninvasive tests such as electrocardiograph (ECG), stress test, eco-stress, nuclide stress test, single photon emission computed tomography (SPECT), or computerized tomography(CT); or invasive test such as coronary angiography. The personal information of the patients was concealed. For patients with several admissions, only data regarding the first admission were valid, unless the data were missing. Two researchers collected the data independently and cross-checked the information to ensure the accuracy of our data.

Statistical analyses

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA), and R version 4.1.3 (R Foundation for Statistical Computing, Vienna, Austria). Multiple imputations were used to fill the predictors for variables with missing data. Normally distributed quantitative data are expressed as the mean with standard deviation, while Student's *t*-test was used to detect differences. Nonnormally distributed quantitative data are presented as the median (P25–P75), while the Mann–Whitney *U* test was used to detect differences. Qualitative data are expressed as *n* (%) and were compared using the Chi-square test or Fisher's exact test. Univariate and multivariate logistic regression analyses were performed to develop a predictive model for the occurrence of CAD in patients with diabetes, whereas the backward stepwise method was employed as the screening method. The area under the receiver-operating characteristic curve (AUC) and its 95% confidence interval (CI) were employed to assess the accuracy of the predictive model. The Brier score and calibration curve were computed to assess the model's predictive value. A nomogram was established based on the predictive model. Statistical significance was set at $P < 0.05$.

Ethical approval of studies and informed consent

This retrospective study was conducted at XXX and was approved by the Ethics Committee of XXX (approval no. 20210055). The study procedures were conducted in accordance with the ethical standards of the Declaration of Helsinki. The requirement for obtaining informed consent was waived because this was a retrospective study that used routinely collected data, and inclusion in the study was not associated with any risk for the patients.

Results

Clinical characteristics

We collected data on 1596 patients between 1 January 2020 and 10 June 2020, among whom 26 patients were diagnosed with gestational diabetes, 23 were aged <18 years, and 157 had missing data, thus allowing 1390 patients to be included in the study. Data for 1152 patients collected before 15 May 2020 served as the training set, whereas the remaining 238 constituted the validation set. In the training set, the CAD incidence was 23.3%, 80.6% of patients were treated with medicine, 17.9% with percutaneous coronary intervention (PCI), and 1.5% with coronary artery bypass surgery (CABG). Their mean age was 55.37 ± 13.62 years, the median history of DM was 7 (2–14) years, and 734 (63.7%) were men. Nonetheless, in the validation set, the CAD incidence was 27.7%, 77.3% of patients were treated with medicine, 21.2% with PCI, and 1.5% with CABG. Their mean age was 57.59 ± 13.64 years, the median history of DM was 7.5 (2–15) years, and 144 (60.7%) were men. The demographics, metabolic factors, and laboratory parameters of patients in the training and validation sets are shown in Table 1, which displays the baseline characteristics of the participants.

Predictive model for coronary artery disease in patients with diabetes mellitus

The univariate analyses performed in the training set showed that age, sex, heart rate, hypertension, diabetes duration, alcohol, smoking, RBC, WCC, HB, serum albumin, GLB, APOA1, APOB100, alanine transaminase, TC, LDL, blood urea, CYC, INR, FT3, and fibrinogen

Table 1 Baseline characteristics of the participants

Variables	Training set ($n=1152$)	Validation set ($n=238$)
Demographics		
Age (years)	55.37 ± 13.62	57.59 ± 13.64
Sex (male)	734 (63.7%)	144 (60.5%)
Metabolic factors		
BMI (kg/m^2)		
≤25	466 (40.5%)	110 (46.2%)
>25	686 (59.5%)	128 (53.8%)
Heart rate (beats/min)	82.64 ± 11.25	81.38 ± 10.60
Hypertension	611 (53.0%)	127 (53.4%)
Diabetes duration (years)	7 (2–14)	7.5 (2–15)
Alcohol	385 (33.4%)	77 (32.4%)
Smoking	412 (35.8%)	72 (30.3%)
Laboratory parameters		
RBC, 10^{12}/l	4.42 ± 0.67	4.43 ± 0.69
WBC, 10^9/l	6.66 ± 2.00	6.59 ± 1.98
Platelets, 10^9/l	219.48 ± 67.53	223.02 ± 74.26
HB, g/l	131.97 ± 20.90	132.58 ± 21.02
ALT, U/l	19.6 (14–29.3)	18.4 (14–31.93)
AST, U/l	18.9 (15.7–24.6)	19.2 (15.28–24.28)
TBIL, μmol/l	10.52 ± 5.23	10.78 ± 5.48
DBIL, μmol/l	3.35 ± 1.54	3.19 ± 1.41
Albumin, g/l	41.05 ± 5.94	41.43 ± 5.92
Globulin, g/l		
<20	163 (14.1%)	32 (13.4%)
≥20	989 (85.9%)	206 (86.6%)
APOA1, g/l	1.08 ± 0.22	1.11 ± 0.22
APOB100, U/l	0.96 ± 0.47	0.91 ± 0.43
Urea, mmol/l	5.70 (4.65–7.22)	5.90 (4.64–7.38)
UA, μmol/l	304.75 ± 90.62	308.76 ± 89.99
RbP, mg/l		
<25.0	71 (6.2%)	8 (3.4%)
25.0–70.0	1029.0 (89.3%)	219.0 (92.0%)
≥20.0	52.0 (4.5%)	11.0 (4.6%)
PT, s	11.76 ± 1.03	11.91 ± 0.93
INR	0.87 (0.80–0.93)	0.90 (0.85–0.96)
FIB, g/l		
<4	875.0 (76.0%)	185.0 (77.7%)
≥4	277.0 (24.0%)	53.0 (22.3%)
FT3, pmol/l	4.08 ± 0.98	4.23 ± 0.92
FT4, pmol/l	15.86 ± 3.39	16.19 ± 3.65
TSH, mIU/l	2.24 (1.48–3.48)	2.35 (1.46–3.54)
CO_2, mmol/l	24.93 ± 2.73	25.05 ± 2.48
TC, mmol/l		
<5.17	797.0 (69.2%)	166.0 (69.7%)
≥5.17	355.0 (30.8%)	72.0 (30.3%)
TG, mmol/l		
<1.7	651.0 (56.5%)	126.0 (52.9%)
≥1.7	501.0 (43.5%)	112.0 (47.1%)
CREA, μmol/l		
<104.0	1037 (90.0%)	215.0 (90.3%)
≥104.0	115 (10.0%)	23.0 (9.7%)
CYC, mg/l		
<1.05	835.0 (72.5%)	170.0 (71.4%)
≥1.05	317.0 (27.5%)	68.0 (28.6%)
LDL, mmol/l		
<1.9	221.0 (19.8%)	54.0 (22.7%)
≥1.9	931.0 (80.8%)	184.0 (77.3%)
HDL, mmol/l		
<1.2	824.0 (71.5%)	168.0 (70.6%)
≥1.2	328.0 (28.5%)	70.0 (29.4%)

ALT, alanine transaminase; APOA1, apolipoprotein A1; APOB100, apolipoprotein B100; AST, aspartate aminotransferase; BMI, body mass index; CREA, creatinine; CYC, cystatin C; DBIL, direct bilirubin; FIB, fibrinogen; FT3, free triiodothyronine; FT4, free tetraiodothyronine; HB, haemoglobin; HDL, high-density lipoprotein; INR, international normalised ratio; LDL, low-density lipoprotein; PT, prothrombin time; RBC, red blood cell; RbP, retinol-binding protein; TBIL, total bilirubin; TC, total cholesterol; TG, triglycerides; TSH, thyroid-stimulating hormone; UA, urinalysis; WBC, white blood cell.

were potential predictive factors for CAD in patients with DM ($P<0.05$), as shown in Table 2, which displayed the findings of patients with DM who did or did not develop CAD in the training set. Twenty-nine variables were included in the multivariable logistic regression analysis, and eight factors remained significant in the final model, including age [odds ratio (OR) 1.58, 95% CI 1.38–1.80, $P<0.001$], sex (OR 1.34, 95% CI 0.98–1.84, $P=0.067$), heart rate (OR 0.86, 95% CI 0.75–1.00, $P=0.040$), hypertension (OR 1.41, 95% CI 1.02–1.94, $P=0.036$), diabetes duration (OR 1.03, 95% CI 1.01–1.05, $P=0.006$), LDL (OR 0.49, 95% CI 0.35–0.69, $P<0.001$), HDL (OR 0.65, 95% CI 0.46–0.93, $P=0.017$), and CREA (OR 1.63, 95% CI 1.04–2.56, $P=0.032$), as shown in Table 3, which displays the univariate and multivariate analysis results of CAD-associated factors in patients with DM.

Nomogram construction and validation

A total of eight variables, including sex, diabetes duration, LDL, CREA, HDL, hypertension, and heart rate, were incorporated to construct a predictive model, which was subsequently visualized by a nomogram. Total scores were computed by summing individual scores and used to predict the probability of CAD (Fig. 1). We used the AUC to assess the accuracy of the predictive model and a plot calibration curve to assess its predictive value. The AUCs were 0.752 (95% CI 0.720–0.784) and 0.738 (95% CI 0.668–0.808) in the training and validation sets, respectively (Fig. 2a and b). The model's sensitivity and specificity values were 0.731 and 0.650 in the training cohort and 0.712 and 0.686 in the validation cohort, respectively. The calibration curves revealed a good fit of the model for predicting the prevalence of CAD in patients with DM, while the Brier scores were 0.153 and 0.172 in the training and validation sets, respectively (Fig. 2c and d).

Discussion

Predictive model for coronary artery disease in patients with diabetes mellitus

From a cohort of 1390 patients diagnosed with DM, we developed a predictive model for CAD in patients with DM based on 54 variables, including demographics, physical examination findings, and laboratory test results, to comprehensively assess the risks. Risk factors that were identified as primarily independent were old age, female sex, hypertension, diabetes duration, and CREA, whereas heart rate, LDL, and HDL were identified as protective factors against CAD in patients with DM. We incorporated these eight variables to develop a nomogram that can help clinicians to easily identify high-risk patients. The AUC, Brier score, and calibration curve results in both the testing and validation sets revealed that our predictive model demonstrated a favourable performance and could be effectively used in clinical practice.

The Framingham Risk Score for coronary heart disease (CHD) is a common and useful tool for estimating the 10-year morbidity risk of CHD in healthy individuals. Apart from the Framingham Risk Score, several prediction

Table 2 Findings among patients with DM who did or did not develop CAD in the training set

Variables	NCAD ($n=884$)	CAD ($n=268$)	$t/x^2/z$	P
Age (years)	53.05 ± 13.32	63.03 ± 11.67	11.04	<0.001
Sex				
Male	581 (79.2%)	153 (20.8%)	6.63	0.010
Female	303 (72.5%)	115 (27.5%)		
Heart rate (beats/min)	83.41 ± 11.30	80.09 ± 10.72	4.25	<0.001
Hypertension				
Absence	455 (84.1%)	86 (15.9%)	31.01	<0.001
Presence	429 (70.2%)	182 (29.8%)		
Diabetes duration (years)	6 (1–12)	10 (5–18)	7.45	<0.001
Alcohol (presence/absence)				
No	572 (74.6%)	195 (25.4%)	6.00	0.014
Yes	312 (81.0%)	73 (19.0%)		
Smoking (presence/absence)				
No	559 (75.5%)	181 (24.5%)	1.66	0.20
Yes	325 (78.9%)	87 (21.1%)		
RBC, 10^{12}/l	4.47 ± 0.65	4.24 ± 0.72	4.65	<0.001
WBC, 10^9/l	6.61 ± 2.00	6.82 ± 2.01	1.51	0.131
HB, g/l	133.4550 ± 20.28	126.93 ± 22.14	4.33	<0.001
Albumin, g/l	42.0 (38.7–45.4)	40.85 (36.6–44.15)	3.98	<0.001
Globulin, g/l				
<20.0	138.0 (84.7%)	25.0 (15.3%)	6.68	0.010
≥20.0	746.0 (75.4%)	243.0 (24.6%)		
APOA1, g/l	1.09 ± 0.23	1.05 ± 0.22	2.16	0.031
APOB100, U/l	0.98 ± 0.47	0.88 ± 0.475	3.30	0.001
ALT, U/l	19.7 (14.03–30.1)	19.0 (14.0–26.0)	1.70	0.089
AST, U/l	19.0 (15.63–25.28)	18.75 (15.8–23.58)	1.05	0.293
TBIL, μmol/l	9.7 (7–13.3)	8.85 (6.5–12.8)	2.02	0.044
TC, mmol/l				
<5.17	593.0 (74.4%)	204.0 (25.6%)	7.88	0.005
≥5.17	291.0 (82.0%)	64.0 (18.0%)		
LDL, mmol/l				
<1.9	136.0 (61.5%)	86.0 (38.5%)	35.38	<0.001
≥1.9	748.0 (80.3%)	183.0 (19.7%)		
HDL, mmol/l				
<1.2	617.0 (74.9%)	207.0 (25.1%)	5.59	0.018
≥1.2	267.0 (81.4%)	61.0 (18.6%)		
Urea, mmol/l	5.64 (4.6–7.00)	6.16 (4.79–8.06)	3.02	0.003
CREA, μmol/l				
<104.0	815.0 (78.6%)	222.0 (21.4%)	20.05	<0.001
≥104.0	69.0 (60.0%)	46.0 (40.0%)		
UA, μmol/l	302. 31 ± 89.12	312.78 ± 95.10	1.66	0.098
PT, s	11.73 ± 1.01	11.87 ± 1.08	1.96	0.050
RbP, mg/l				
<25.0	59.0 (83.1%)	12.0 (16.9%)	2.53	0.282
25–70.0	788.0 (76.6%)	241.0 (23.4%)		
≥20.0	37.0 (71.2%)	15.0 (28.8%)		
CYC, mg/l				
<1.05	674.0 (80.7%)	161.0 (19.3%)	26.96	<0.001
≥1.05	210.0 (66.2%)	107.0 (33.8%)		
INR	0.87 (0.80–0.92)	0.89 (0.82–0.94)	2.64	0.008
FT3, pmol/l	4.13 ± 0.97	3.92 ± 0.97	3.07	0.002
FIB, g/l				
<4.0	690.0 (78.9%)	185.0 (21.1%)	9.17	0.002
≥4.0	194.0 (70.0%)	83.0 (30.0%)		

ALT, alanine transaminase; APOA1, apolipoprotein A1; APOB100, apolipoprotein B100; AST, aspartate aminotransferase; CREA, creatinine; CYC, cystatin C; FIB, fibrinogen; FT3, free triiodothyronine; HB, haemoglobin; HDL, high-density lipoprotein; INR, international normalised ratio; LDL, low-density lipoprotein; PT, prothrombin time; RBC, red blood cell; RbP, retinol-binding protein; TBIL, total bilirubin; TC, total cholesterol; UA, urinalysis; Urea, blood urea; WBC, white blood cell.

models, such as the GRACE, TIMI, SYNTAX, and CRUSADE models, have been developed to assess the general risk of CAD; however, none of them is able to evaluate the risk of CAD in patients with DM.[12–14] To the best of our knowledge, this is the first predictive model to be developed for CAD incidence in patients with DM. Besides, our predictive model includes the variable of diabetes duration, which means it could predict the risk of CAD at 5, 10, or more years from the diagnosis of DM. In addition, the sample size of this study was 1390 cases, which is relatively large compared with similar studies, thus solidifying the credibility of the results. In accordance with other models, our prediction model elucidated the adverse effects of old age and hypertension in CAD in patients with DM.

Study variables

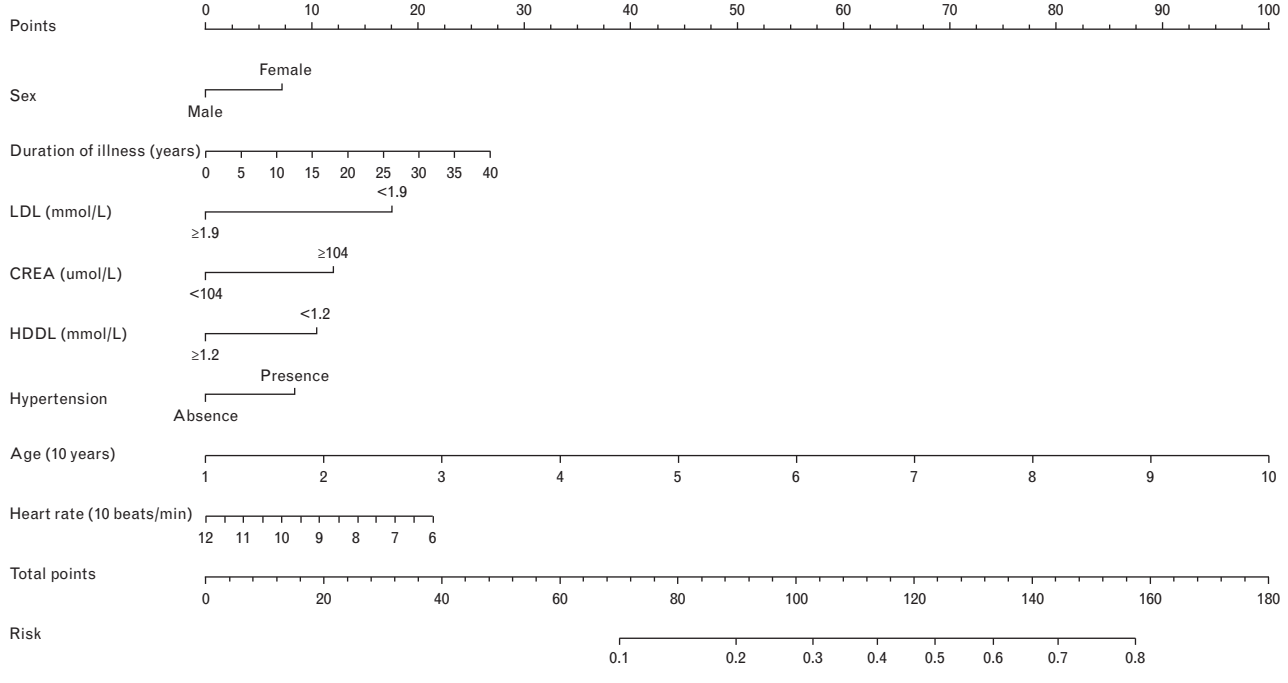
The involvement of DM in the development of coronary artery atherosclerosis has become more progressive and severe, but less prognostic than before. Early screening of

Table 3 Univariate and multivariate analyses of factors associated with CAD in patients with DM

	Univariate analysis				Multivariate analysis			
Variables	OR	95% CI	χ^2	*P*	OR	95% CI	χ^2	*P*
Age (years)	1.85	1.64–2.09	99.66	<0.001	1.58	1.38–1.80	43.60	<0.001
Sex (female/male)	1.44	1.09–1.91	6.60	0.010	1.34	0.98–1.84	3.44	0.064
Heart rate (BPM)	0.76	0.66–0.86	17.51	<0.001	0.86	0.75–1.00	4.05	0.040
Hypertension (presence/absence)	2.25	1.68–3.00	30.19	<0.001	1.41	1.02–1.94	4.41	0.036
Diabetes duration (years)	1.07	1.05–1.08	52.10	<0.001	1.03	1.01–1.05	7.65	0.006
Alcohol (presence/absence)	0.69	0.51–0.93	5.96	0.015				
Smoke (presence/absence)	0.83	0.62–1.11	1.65	0.198				
RBC, 10^{12}/l	0.61	0.50–0.75	23.19	<0.001				
WBC, 10^9/l	1.05	0.99–1.12	2.28	0.131				
HB, g/l	0.99	0.98–0.99	19.85	<0.001				
Albumin, g/l	0.96	0.93–0.98	15.80	<0.001				
Globulin (high/low)	1.80	1.15–2.82	6.53	0.011				
APOA1, g/l	0.51	0.28–0.94	4.62	0.032				
APOB100, U/l	0.57	0.40–0.80	10.63	0.001				
ALT, U/l	0.99	0.98–1.00	4.98	0.026				
AST, U/l	0.99	0.98–1.01	1.33	0.250				
TBIL, μmol/l	0.98	0.95–1.01	2.26	0.133				
TC (high/low)	0.64	0.47–0.88	7.80	0.005				
LDL (high/low)	0.39	0.29–0.54	33.94	<0.001	0.49	0.35–0.69	16.97	<0.001
HDL (high/low)	0.68	0.50–0.94	5.55	0.018	0.65	0.46–0.93	5.68	0.017
Urea, mmol/l	1.05	1.02–1.09	11.40	0.001				
CREA (high /low)	2.45	1.64–3.66	19.09	<0.001	1.63	1.04–2.56	4.59	0.032
UA, μmol/l	1.00	1.00–1.00	2.74	0.098				
PT, s	1.14	1.00–1.30	3.81	0.051				
RbP (high/moderate/low)	1.37	0.90–2.09	2.12	0.145				
CYC (high/low)	2.13	1.60–2.85	26.32	<0.001				
INR	4.33	1.37–13.70	6.22	0.013				
FT3, pmol/l	0.81	0.71–0.93	9.24	0.002				
FIB (high/low)	1.60	1.18–2.16	9.08	0.003				

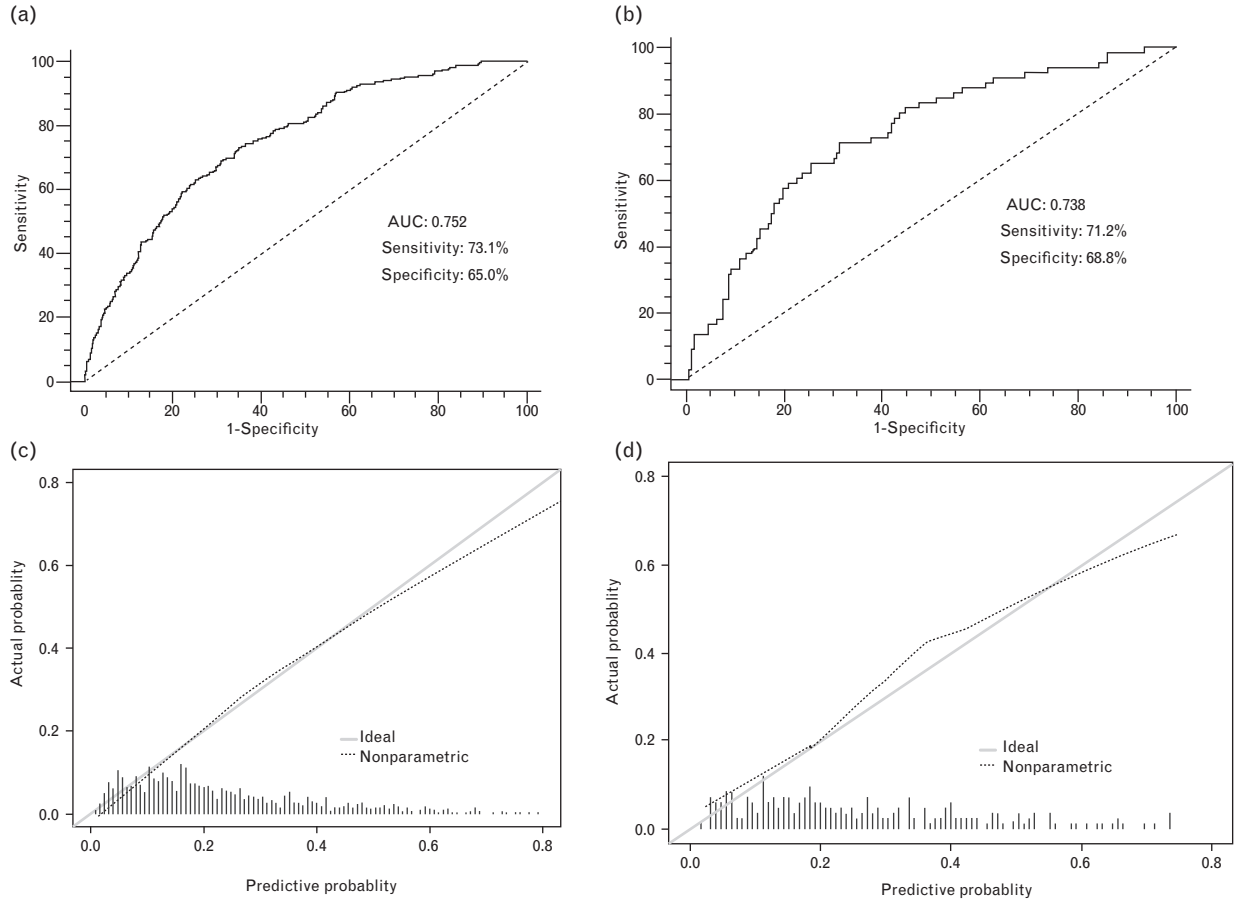
ALT, alanine transaminase; APOA1, apolipoprotein A1; APOB100, apolipoprotein B100; AST, aspartate aminotransferase; CREA, creatinine; CYC, cystatin C; FIB, fibrinogen; FT3, free triiodothyronine; HB, haemoglobin; HDL, high-density lipoprotein; INR, international normalised ratio; LDL, low-density lipoprotein; PT, prothrombin time; RBC, red blood cell; RbP, retinol-binding protein; TBIL, total bilirubin; TC, total cholesterol; UA, urinalysis; Urea, blood urea; WBC, white blood cell.

Fig. 1



Nomogram risk score plot of predictors of CAD in patients with DM. CAD, coronary artery disease; DM, diabetes mellitus.

Fig. 2



Receiver-operating characteristic curves based on eight predictors for the predictive model: training cohort (a) and validation cohort (b). Calibration curve plot of the model in the test cohort (c) and validation cohort (d). AUC, area under the receiving operating characteristic curve.

high-risk individuals potentially alerts them of the need to modify their lifestyles or alter their treatment to prevent the occurrence of CAD. Older people are more susceptible to increased oxidative molecular mediators and decreased antioxidative factors,[15] which can aggravate the development of CAD. Moreover, hypertension exacerbates atherosclerosis and increases the risk of CAD by producing oxygen-free radicals and recruiting inflammatory cells into the arterial wall.[16] Furthermore, individuals with a longer duration of DM are more prone to CAD. Hyperglycaemia can potentially induce various signalling pathways that aggravate inflammation, accelerate calcium deposition, and exacerbate the apoptosis of vascular smooth muscle, thus contributing to the development of CAD.[17]

Although several studies have indicated that tachycardia aggravates inflammation, increases oxidative stress, and worsens patients' prognosis,[18,19] the SIGNIFY trial[20] reported that tachycardia is merely a marker of DM, which influences CAD progression, rather than a risk factor. In our study, we found that patients with diabetes who had decreased heart rates had worsened outcomes: a finding that may be consistent with that of the SIGNIFY trial.[20] Oxygen-free radicals and antioxidant defence systems are imbalanced in patients with diabetes and negatively affect the valgus and sympathetic nervous system, which regulates the heart. This results in increased cardiac load, while a low heart rate would enlarge myocardial ischemic injury and accelerate the progress of CHD.[21]

Regarding the sex, our model yielded slightly different results from those of the Framingham Risk Score, possibly due to the different patient age ranges. HDL potentially generates a protective effect against CAD, by stimulating endothelial-cell nitric oxide production and promoting endothelial-cell repair mechanisms;[22,23] HDL demonstrated a similar protective effect against CAD in patients with DM. A high level of LDL-cholesterol (LDL-C) is an established risk factor for CAD in healthy individuals.[24] Our model explored the association

between LDL-C and CAD in patients with DM and found that the level of LDL-C in CAD is slightly lower than that in individuals without CAD, which is relatively consistent with the findings of Bittencourt *et al.*[25] and might be explained by phytosterols. Many diabetic patients have accompanying dyslipidaemia. Phytosterols act as dietary supplements added to milk, soy, and yoghurt. It could decrease intestinal absorption of cholesterol and reduce LDL-cholesterol, whereas it increases the deposition of sterol in cardiovascular tissue and enhances organ damage which might increase the incidence of CAD.[26,27] Chronic kidney disease shows abnormal calcium-phosphorus metabolism and oxidative stress and increases CAD risk.[28] CREA, a known marker of renal function was associated with a high risk of CAD in patients with DM.

Limitations

We developed a predictive model for CAD in patients with DM. Nonetheless, certain limitations need to be addressed in clinical practice. First, our model was developed based on a retrospective study. Second, only temporal external validation was performed without including any external spatial validation.

Conclusions

In conclusion, among other variables, our predictive model had incorporated sex, diabetes duration, HDL, LDL, CREA, hypertension, and heart rate, with demonstrated favourable performance, both internally and externally. Thus, it could be effectively used in clinical practice for predicting the incidence of CAD in patients with DM.

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Data availability statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Conflicts of interest

There are no conflicts of interest.

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