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Factors associated with the severity of coronary artery disease in type 2 diabetes mellitus patients

ZHU Baohua, SUN Yanjun, LI Min
Department of General Practice, Jinan People's Hospital, Jinan, Shandong 271100, China

Abstract: Objective To analyze the factors related to the severity of coronary artery disease (CAD) in type 2 diabetes mellitus (T2DM) patients, with the aim of providing a reference for the risk assessment of them. **Methods** Clinical data of 322 T2DM patients combined with CAD admitted to Jinan People's Hospital from January 2019 to May 2023 were retrospectively analyzed. They were divided into the mild group and the moderate to severe group based on the Gensini score. The clinical data of age, gender, and blood indexes between the two groups were compared. Least absolute shrinkage and selection operator (LASSO)and logistic regression analysis were used to screen for factors correlated with the severity of coronary artery lesions in T2DM patients. The prediction model was established, the model calibration curve and the receiver operating characteristic curve (ROC) were drawn, and the area under the curve (AUC) was calculated to evaluate its accuracy. **Results** Age, total cholesterol, fasting blood glucose, remnant cholesterol and lipoprotein(a) levels were higher in the moderate to severe group than those in the mild group (P<0.05).For patients with moderate to severe coronary artery lesions in T2DM, the multivariate logistic regression analysis showed that age, residual cholesterol and serum lipoprotein α levels were independent risk factors (P<0.05), and the LASSO regression showed age (Z=3.251, P=0.001), residual cholesterol (Z=7.989, P<0.001) and serum lipoprotein α levels (OR=2.565, P=0.030) were its independent predictor, and the column chart prediction model constructed from the above factors had good accuracy (AUC=0.826). **Conclusion** Age, remnant cholesterol and lipoprotein-α levels can effectively predict the severity of coronary artery lesions in T2DM patients, and has good accuracy.
Keywords: Type 2 diabetes mellitus; Coronary artery disease; Age; Remnant cholesterol; Lipoprotein(a)
Fund program: Shandong Province Medical and Health Technology Development Plan (2019WS0660)

In 2017, global data indicated approximately 451 million patients with type 2 diabetes mellitus (T2DM), with projections suggesting an increase to 693 million by 2045 [1]. Census data from 2020 showed China's population aged 60 and above to be about 260.4 million, among whom approximately 30% suffer from T2DM [2]. T2DM is an independent risk factor for coronary artery disease (CAD); statistics indicate that T2DM patients have twice the risk of developing CAD and CAD-related mortality compared to non-T2DM individuals [3-4]. Current research suggests that the pathogenesis of T2DM combined with CAD may involve vascular endothelial cell damage and abnormalities in lipid metabolism due to hyperglycemia [5].The Gensini score is commonly used to assess the severity of CAD lesions, but it relies on invasive coronary angiography results. Therefore, there is a need for non-invasive tools to evaluate the severity of CAD in T2DM patients. This study aims to explore the factors associated with the severity of CAD in T2DM patients to provide insights for risk assessment in those with T2DM and concurrent CAD.

1 Material and methods

1.1 General information

A retrospective review included 322 T2DM patients with concurrent CAD admitted to Jinan People's Hospital from January 2019 to May 2023. **Inclusion criteria**: (1) Diagnosis of T2DM according to established criteria [6]; (2) Confirmation of CAD by coronary angiography; (3) Complete medical records. **Exclusion criteria:** (1) Severe hepatic or renal dysfunction, psychiatric disorders; (2) Malignant tumors; (3) Severe hypoglycemic or hyperglycemic states in the three months prior to admission.

Patients were categorized into mild and moderate-severe groups based on Gensini scores calculated from coronary angiography results, with a median score of 54 as the threshold [7]. This study was approved by the Ethics Committee, Approval No. JYLU2023-007.

1.2 Data collection

General information was collected, including gender, age, body mass index (BMI), duration of T2DM, and CAD. Admission blood indices was collected, including serum levels of small dense low-density lipoprotein cholesterol (sdLDL-C), glycated hemoglobin (HbA1c), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), lipoprotein(a) [Lp(a)], hypersensitive C-reactive protein (hsCRP), and fasting plasma glucose (FPG). Residual cholesterol (RC) level was calculated based on TC, LDLC, and HDLC levels [7]. The triglyceride-glucose index (TyG) was calculated based on TG, HDLC, and FPG levels [8].

1.3 Statistical methods

SPSS 26.0 software was used for data analysis. Normally distributed continuous variables are presented as mean ± standard deviation ($\bar{x} \pm s$), and independent sample *t*-tests were used for comparisons between groups. Non-normally distributed variables are presented as $M (Q_1, Q_3)$, and the Mann-Whitney U test was applied for between-group comparisons. Categorical variables are presented as case, and comparisons between groups were performed using chi-square tests or non-parametric tests. Factors showing significant differences between groups were included in multivariate logistic regression analysis to identify independent risk factors, with $P<0.05$ indicating statistical significance. The least absolute shrinkage and selection operator (LASSO) regression method was used to select the optimal predictive factors for assessing the severity of coronary artery lesions in T2DM patients. Predictive models were established using R language, and calibration curves and receiver operating characteristic (ROC) curves were plotted to evaluate model accuracy.

2 Results

2.1 Comparison of general data

The mild group included 177 patients, and the moderate-severe group included 145 patients. There was no statistically significant difference between groups in terms of gender, duration of T2DM, duration of CAD, or BMI ($P>0.05$). However, there was a significant difference in age between the two groups ($P<0.01$). **See Tab.1.**

Tab. 1 Comparison of general information between two groups

Indicator	mild group (*n*=177)	moderate-severe group (*n*=145)	$t/Z/\chi^2$	*P*
Age(years)[a]	64.5±7.6	68.5±7.6	22.274	< 0.001
Gendet[case(%)]				
male	98 (55.4)	74 (51)	0.601	0.438
female	79 (44.6)	71 (49)		
T2DM course(years)[b]	8.0 (4.0, 12.0)	9.0 (4.0, 13.0)	3.808	0.051
CAD course(years)[b]	5.0 (2.0, 8.0)	5.0 (3.0, 8.0)	0.504	0.478
BMI(kg/m²)[a]	25.9±4.4	25.6±4.4	0.380	0.538

Note:[a] represented as $\bar{x} \pm s$; b represented as $M(Q_1,Q_3)$.

2.2 Comparison of blood indices between two groups

Significant differences between the mild and moderate-severe groups were observed in FPG, TC, RC, and Lp(a) levels ($P<0.05$). No significant differences were found in hsCRP, HbA1c, TG, sdLDL-C, HDL-C, LDL-C, or TyG levels ($P>0.05$). **(Tab.2)**

2.3 Analysis of factors influencing the severity of CAD in patients with T2DM

By conducting a multi-factor logistic regression analysis with age, FPG, TC, Lp(a), and RC levels showing significant differences between groups as independent variables and using moderate to severe disease (Gensini score>54) as the dependent variable, the results indicated that older age, high Lp(a), and RC levels were independent risk factors for severe CAD in T2DM patients. **(Tab.3)**

Tab.2 Comparison of blood indices between the patients in two groups

Indicator	mild group (*n*=177)	moderate-severe group (*n*=145)	*t/Z*	*P*
hsCRP(mg/L)[a]	28.0 ± 16.6	30.1 ± 17.2	1.231	0.268
sdLDL-C (mmol/L)[b]	1.0 (0.5, 1.3)	1.0 (0.4, 1.5)	0.001	0.989
HbA1c[a]	8.2 ± 2.6	7.8 ± 2.3	1.697	0.194
TC(mmol/L)[b]	5.3 (4.3, 6.8)	5.9 (4.5, 7.7)	5.021	0.025
TG(mmol/L)[b]	2.6 (1.4, 3.7)	2.6 (1.4, 4.0)	0.209	0.648
HDL-C (mmol/L)[b]	1.9 (1.4, 2.5)	1.7 (1.3, 2.4)	1.432	0.231
LDL-C (mmol/L)[b]	2.2 (1.2, 3.4)	2.3 (1.0, 3.2)	0.651	0.420
Lp(a)(mg/L)[b]	263.2 (161.3, 346.2)	451.6 (284.7, 543.8)	85.147	<0.001
FPG(mmol/L)[a]	10.4 ± 3.6	11.3 ± 3.3	4.947	0.027
RC(mmol/L)[a]	1.4 ± 0.6	1.7 ± 0.6	13.372	<0.001
TyG[a]	9.6 ± 1.0	9.8 ± 0.9	1.607	0.206

Note:[a] represented as $\bar{x} \pm s$; b represented as $M(Q_1,Q_3)$.

Tab.3 Factors influencing the severity of coronary artery lesions in patients with T2DM

Indicator	*β*	*SE*	*Wald*	*P*	*OR*	95%*CI*
Age	0.061	0.019	10.773	0.001	1.063	1.025-1.102
FPG	0.061	0.041	2.186	0.139	1.063	0.980-1.152
TC	0.036	0.080	0.201	0.654	1.037	0.886-1.213
Lp(a)	0.009	0.001	62.437	<0.001	1.009	1.007-1.012
RC	0.574	0.264	4.724	0.030	1.775	1.058-2.977

2.4 Selection of optimal predictive factors for the severity of CAD in T2DM Patients

Lasso regression results revealed that age, Lp(a), and RC levels were the best predictive factors for severe CAD in T2DM patients, consistent with the results of the multi-factor logistic regression analysis. **(Tab.4 and Fig.1)**

Tab. 4 Best predictors of coronary artery lesions severity in patients with T2DM

Indicator	Estimate	Standard Deviation	*Z* value	*P* value
Age	0.061	0.019	3.251	0.001
FPG)	0.069	0.042	1.659	0.097
TC	-0.432	0.225	-1.917	0.055
Lp(a)	0.009	0.001	7.989	<0.001
RC	0.631	0.246	2.565	0.010

2.5 Construction of a Prediction Model for the Severity of CAD in T2DM Patients

Using the "rms" and "regplot" packages in R language (version 4.1.2), a prediction model was constructed using age, RC, and Lp(a) as variables. A scoring formula was developed, and a column plot **(Fig.2)** was created. By calculating the scores for each risk factor and summing these scores for individual patients, the severity of coronary artery disease in T2DM patients can be evaluated based on the total score **(Tab.5)**.

Tab.5 Grading formula of the predictors

Variable	formula
Age	1.050 198 137×Age-54.610 303 105
Lp(a)	0.153 846 154×Lp(a) -7.692 307 692
RC	10.508 359 349×RC-2.101 671 870

2.6 Evaluation of the accuracy of the column plot model

The model calibration curve closely aligns with the actual curve **(Fig.3A)**. The area under the roc curve (AUC) to validate the model accuracy was found to be 0.826 **(Fig.3B)**.

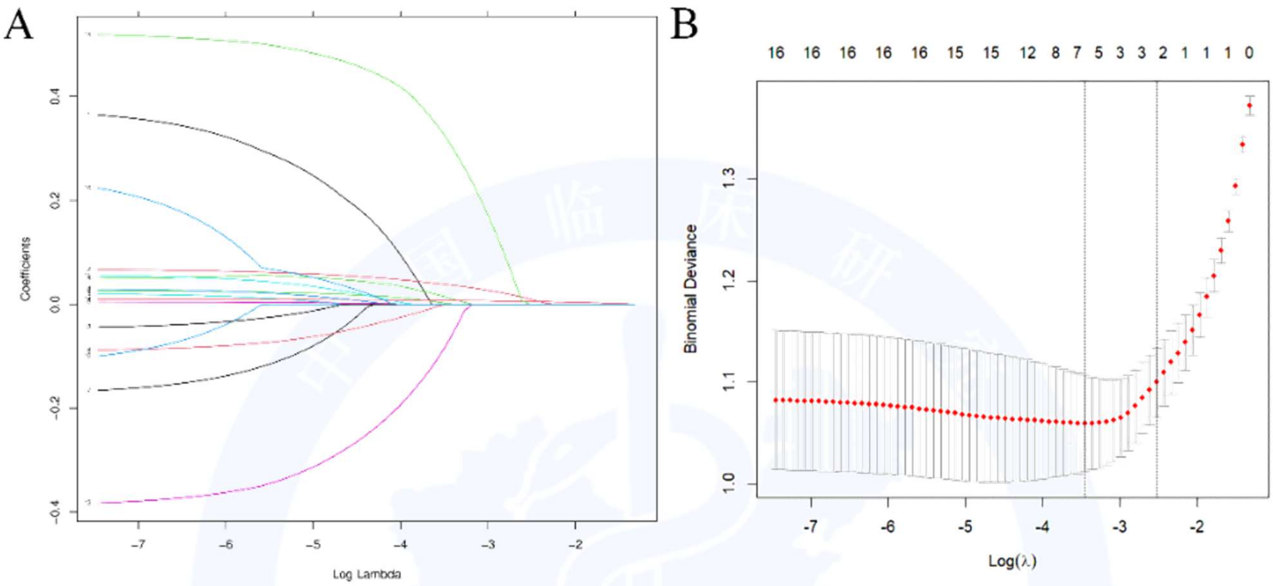

Fig. 1 LASSO regression screening of the best predictors of coronary artery lesions severity in T2DM patients

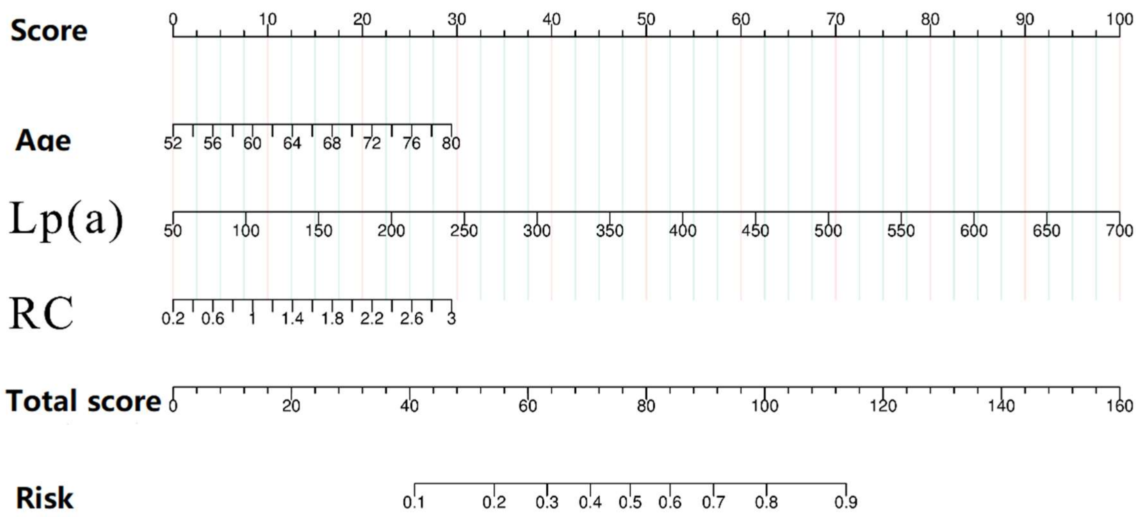

Fig.2 Nomogram of the predictive model of coronary artery lesions severity in patients with T2DM

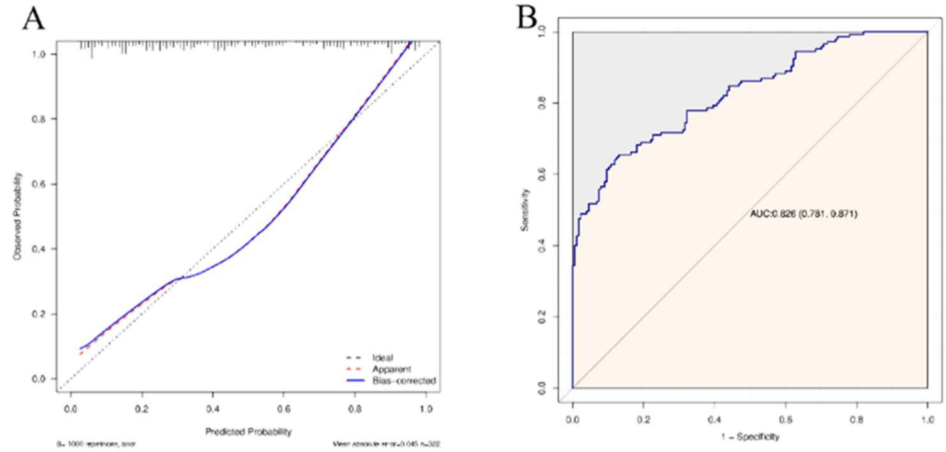

Fig. 3 Accuracy evaluation of the nomogram prediction model

3 Discission

Compared with healthy individuals, pathological conditions such as hypertension, obesity, and dyslipidemia are more common in patients with type 2 diabetes mellitus (T2DM), and these factors are also risk factors for coronary artery disease (CAD) [8]. Within the circulatory system, endothelial nitric oxide synthase participates in the regulation of vascular function, with nitric oxide it produces being a key endothelium-dependent vasorelaxant factor. Hyperglycemia reduces the synthesis of endothelial nitric oxide synthase, decreases the bioavailability of nitric oxide, and leads to endothelial dysfunction [9]. High glucose and free fatty acids upregulate the expression of microRNA-34a in vascular endothelial cells, targeting silent information regulator factor 1, inhibiting P53 gene acetylation, enhancing P53 gene and downstream senescence-related gene transcription activities, causing endothelial cell aging, impairing endothelial function, and accelerating the progression of atherosclerosis [10-11]. Under high glucose conditions, advanced glycation end-products accumulate in the body, and through receptor interactions, these products induce arterial wall damage and plaque formation by altering cell activity, promoting gene expression, and increasing the efflux of inflammatory compounds [12]. Furthermore, high glucose levels can alter the structure and function of coronary arteries. Studies have shown that in T2DM patients, there is proliferation of endothelial cells and subendothelial cells in small coronary artery branches, often accompanied by fibrosis [13].

T2DM patients often have concurrent lipid metabolism disorders, another risk factor for CAD. Active intervention targeting dyslipidemia and other CAD risk factors can reduce the incidence of cardiovascular events in T2DM patients [14]. Lp(a) is primarily composed of low-density lipoprotein-like particles complexed with apolipoprotein(a) and apolipoprotein B, with a high content of free fatty acids internally making it more prone to oxidation. Oxidized Lp(a) is more likely to act on arterial endothelial cells, inducing endothelial cell damage [15-16]. Endothelial cells stimulated by oxidized Lp(a) release cytokines and growth factors, inducing monocyte adhesion and transendothelial migration, leading to lipid engulfment in the intima and eventually forming foam cells [17]. This study demonstrated a close correlation between Lp(a) levels and severe coronary artery lesions in T2DM patients. Even after adjusting for age and RC (renin-angiotensin system components), high Lp(a) levels remained an independent predictor of severe coronary artery lesions in T2DM patients, with good accuracy.

The correlation between age and the severity and prognosis of CAD has been confirmed [18]. Research indicated that elderly T2DM patients with CAD (>60 years old) predominantly presented with triple-vessel and diffuse lesions, indicating more severe and complex conditions [19]. This study also confirmed age as an independent predictor of the severity of coronary artery lesions in T2DM patients, with good predictive accuracy.

Previous studies have shown a positive correlation between RC levels and atherosclerosis [20], with RC also being an effective predictor of cardiovascular disease [21]. PREDIMED study found that for every 10 mg/dL increase in RC levels, there is a 21% increased risk of major cardiovascular events, and when RC levels exceed 30 mg/dL, the risk of major cardiovascular events is consistently higher compared to RC levels ≤30 mg/dL, independent of LDL-C levels [22]. Quispe *et al.* [23] found a positive correlation between RC and cardiovascular disease, suggesting RC as a risk factor for acute CAD independent of factors such as LDL-C and ApoB.

This study indicates that advanced age, elevated RC levels, and high Lp(a) levels are independent predictors of severe CAD in T2DM patients. The combined prediction of these factors shows good accuracy in predicting the severity of CAD in T2DM patients. However, due to the relatively small sample size and retrospective nature of this study, the correlation and predictive value of age, RC levels, and Lp(a) levels with the severity of CAD in T2DM patients require further confirmation through larger sample sizes or prospective studies.

The authors report no conflict of interest

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·论　著·

2 型糖尿病患者冠状动脉病变严重程度的相关因素

朱宝华，　孙艳君，　李敏

山东第一医科大学附属人民医院 济南市人民医院全科医学科，山东 济南 271100

摘要：目的　对 2 型糖尿病(T2DM)患者冠状动脉病变严重程度的相关因素进行分析,以期为其风险评估提供参考。**方法**　回顾性分析 2019 年 1 月至 2023 年 5 月济南市人民医院收治的 322 例 T2DM 合并冠状动脉疾病患者的临床资料,根据 Gensini 评分分为轻度组(≤54 分，n=177)和中重度组(>54 分，n=145),对比两组患者的年龄、性别、血液指标等临床资料,采用 logistic 回归分析和最小绝对收缩和选择算子(LASSO)回归法筛选与 T2DM 患者冠状动脉病变严重程度的相关性因素,构建预测模型,绘制模型校准曲线和受试者工作特征曲线(ROC)并计算曲线下面积(AUC)评价其准确性。**结果**　中重度组患者年龄及总胆固醇、空腹血糖、残余胆固醇、血清脂蛋白 a[Lp(a)]水平均高于轻度组患者(P<0.05)。对于 T2DM 患者中重度冠状动脉病变,多因素 logistic 回归分析结果显示年龄(Z=3.251，P=0.001)、残余胆固醇(Z=2.564，P=0.010)和血清 Lp(a)(Z=7.989，P<0.001)水平是其独立危险因素(P<0.05),LASSO 回归结果显示,年龄、残余胆固醇和血清 Lp(a)水平是其独立预测因素(P<0.05),由上述因素构建的列线图预测模型准确性较好(AUC=0.826)。**结论**　年龄、残余胆固醇和血清 Lp(a)水平可有效预测 T2DM 患者冠状动脉病变的严重程度,且准确性较好。

关键词： 2 型糖尿病；冠状动脉病变；年龄；残余胆固醇；脂蛋白 a

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Factors associated with the severity of coronary artery disease in type 2 diabetes mellitus patients

ZHU Baohua, SUN Yanjun, LI Min

Department of General Practice, Jinan City People's Hospital, Affiliated People's Hospital of Shandong First Medical University, Jinan, Shandong 271100, China

Abstract: Objective　To analyze the factors related to the severity of coronary artery disease (CAD) in type 2 diabetes mellitus (T2DM) patients, with the aim of providing a reference for the risk assessment of them. **Methods**　Clinical data of 322 T2DM patients combined with CAD admitted to Jinan City People's Hospital from January 2019 to May 2023 were retrospectively analyzed. They were divided into the mild group (Gensini score≤54, n=177) and the moderate to severe group (Gensini score>54, n = 145) based on the Gensini score. The clinical data of age, gender, and blood indexes between the two groups were compared. Least absolute shrinkage and selection operator (LASSO) and logistic regression analysis were used to screen for factors correlated with the severity of CAD in T2DM patients. The prediction model was established, the model calibration curve and the receiver operating characteristic curve (ROC) were drawn, and the area under the curve (AUC) was calculated to evaluate its accuracy. **Results**　Age, total cholesterol, fasting blood glucose, remnant cholesterol and lipoprotein (a) levels were higher in the moderate to severe CAD in the mild group (P < 0.05). For patients with moderate to severe coronary artery lesions in T2DM, the multivariate logistic regression analysis showed that age, residual cholesterol and serum lipoprotein (a) levels were independent risk factors (P<0.05). LASSO regression showed age (Z = 3.251, P = 0.001), residual cholesterol (Z = 2.565, P = 0.010) and serum lipoprotein (a) levels (Z=7.989, P<0.001) were independent predictor of T2MD patients with moderate to serve CAD, and the column chart prediction model constructed from the above factors had good accuracy (AUC=0.826).

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Conclusion　Age, remnant cholesterol and lipoprotein (a) levels can effectively predict the severity of CAD in T2DM patients, and have good accuracy.

Keywords: Type 2 diabetes mellitus; Coronary artery disease; Age; Remnant cholesterol; Lipoprotein (a)

Fund program: Shandong Province Medical and Health Technology Development Plan (2019WS0660)

2017 年数据显示,全世界约有 4.51 亿 2 型糖尿病(type 2 diabetes mellitus, T2DM)患者,到 2045 年,T2DM 患者人数可增长至6.93 亿[1]。数据显示,2020 年我国 60 岁以上人口约有 2.604 亿,其中约有 30% 罹患 T2DM[2]。T2DM 是冠状动脉疾病(coronary artery disease, CAD)的独立危险因素,据统计,T2DM 患者发生 CAD 的风险和 CAD 相关死亡的风险是非 T2DM 患者的 2 倍[3-4]。现有研究表明,T2DM 合并 CAD 的发病机制可能与高糖状态导致血管内皮细胞损伤、脂质代谢异常相关[5]。Gensini 评分多用于评估 CAD 患者病变的严重程度,但该评分计算基于冠状动脉造影结果,属有创检查,评估 T2DM 患者 CAD 严重程度的工具亟待开发。本研究旨在探索 T2DM 患者 CAD 严重程度的相关性因素,为 T2DM 合并 CAD 患者的风险评估提供参考。

1　资料与方法

1.1　*一般资料*　回顾性选取济南市人民医院 2019 年 1 月—2023 年 5 月收治的 322 例 T2DM 合并 CAD 患者为研究对象。入组标准:(1) 符合 T2DM 诊断标准[6];(2) 已接受冠状动脉造影检查并确诊为合并 CAD 者;(3) 病历资料完整者。排除标准:(1) 合并严重肝、肾功能障碍、精神类疾患者;(2) 合并恶性肿瘤者;(3) 入院前 3 个月出现严重低血糖或高血糖状态。入组患者根据冠状动脉造影结果计算 Gensini 评分,以 Gensini 评分的中位数(54 分)为节点,将 Gensini 评分>54 分的患者纳入中重度组,将 Gensini 评分≤54 分的患者纳入轻度组[7]。本研究已通过伦理委员会批准,批准号:济医伦批第(SWYX: No.2023-007)。

1.2　*资料收集*　收集入组患者的一般资料,包括性别、年龄、体质量指数(body mass index, BMI)、T2DM 病程、CAD 病程;统计入组患者入院血液指标,包括血清小而密低密度脂蛋白胆固醇(small dense low density lipoprotein cholesterol, sdLDL-C)、糖化血红蛋白(glycated hemoglobin, HbA1c)、总胆固醇(total cholesterol, TC)、三酰甘油(triglycerides, TG)、高密度脂蛋白胆固醇(high density lipoprotein cholesterol, HDL-C)、低密度脂蛋白胆固醇(low density lipoprotein cholesterol, LDL-C)、脂蛋白 a[lipoprotein (a), Lp(a)]、超敏 C 反应蛋白(hypersensitive C-reactive protein, hsCRP)、空腹血糖(fasting plasma glucose, FPG)水平等;根据 TC、LDL-C 和 HDL-C 水平计算残余胆固醇(remnant cholesterol, RC)水平[7];根据 TG、HDL-C 和 FPG 水平计算三酰甘油-葡萄糖指数(triglyceride-glucose, TyG)[8]。

1.3　*统计学方法*　所有数据采用 SPSS 26.0 统计软件进行分析。计量资料符合正态分布的以 $\bar{x}\pm s$ 表示,两组间比较采用独立样本 t 检验;不符合正态分布的以 $M(Q_1, Q_3)$表示,两组间比较应用 Mann-Whitney U 检验;计数资料用(例)表示,组间比较采用χ^2 检验或非参数秩和检验;组间比较有显著差异的因素代入多因素 logistic 回归分析进行独立危险因素检验,以 $P<0.05$ 表示差异有统计学意义。采用最小绝对收缩和选择算子(least absolute shrinkage and selection operator, LASSO)回归法筛选 T2DM 患者冠状动脉病变严重程度的最佳预测因素,使用 R 语言建立预测模型并绘制列线图,绘制模型的校准曲线和受试者工作特征(receiver operating characteristics, ROC)曲线评价预测模型的准确性。

2　结　果

2.1　*两组患者一般资料比较*　轻度组患者 177 例,中重度组患者 145 例,两组患者性别、T2DM 病程、CAD 病程、BMI 差异无统计学意义($P>0.05$);两组患者年龄差异有统计学意义($P<0.01$)。见表 1。

2.2　*两组患者血液指标比较*　两组患者 FPG、TC、RC、Lp(a)水平差异有统计学意义($P<0.05$);两组患者 hsCRP、HbA1c、TG、sdLDL-C、HDL-C、LDL-C、TyG 水平差异无统计学意义($P>0.05$)。见表 2。

2.3　*T2DM 患者冠状动脉病变严重程度的影响因素分析*　以组间比较有统计学差异的年龄、FPG、TC、Lp(a)和 RC 水平为自变量,以中重度病变(Gensini 积分>54 分)为因变量,进行多因素 logistic 回归分析,结果表明,年龄大、Lp(a)和 RC 水平高是 T2DM 患者中重度冠状动脉病变的独立危险因素。见表 3。

2.4　*T2DM 患者冠状动脉病变严重程度的最佳预测因素筛选*　LASSO 回归结果表明,年龄、Lp(a)和 RC 水平是 T2DM 患者中重度冠状动脉病变的最佳预测

因素，与多因素 logistic 回归分析结果相同。见表 4、图 1。

2.5　T2DM 患者冠状动脉病变严重程度的预测模型构建　使用 R 语言(4.1.2)“rms”“regplot”数据包，将年龄、RC 和 Lp(a)作为变量构建预测模型，制定赋分公式并绘制列线图(图 2)。各危险因素代入公式分别赋分，将患者各因素赋分相加，即可根据总分值评估 T2DM 患者冠状动脉病变的严重程度(表 5)。

2.6　列线图模型的准确性评价　模型校准曲线与实际曲线重合良好(图 3A)。验证模型准确性的 ROC 曲线下面积为 0.826(图 3B)。

表 1　两组患者一般资料比较

Tab. 1　Comparison of general information between the patients in two groups

变量	轻度组 (n=177)	中重度组 (n=145)	$t/\chi^2/Z$ 值	P 值
年龄(岁)[a]	64.5±7.6	68.5±7.6	22.274	<0.001
性别[例(%)]				
男	98 (55.4)	74 (51.0)	0.601	0.438
女	79 (44.6)	71 (49.0)		
T2DM 病程(年)[b]	8.0 (4.0, 12.0)	9.0 (4.0, 13.0)	3.808	0.051
CAD 病程(年)[b]	5.0 (2.0, 8.0)	5.0 (3.0, 8.0)	0.504	0.478
BMI(kg/m^2)[a]	25.9±4.4	25.6±4.4	0.380	0.538

注：[a] 表示数据为 $\bar{x}\pm s$；[b] 表示数据为 $M(Q_1, Q_3)$。

表 2　两组患者血液指标比较

Tab. 2　Comparison of blood indices between the patients in two groups

变量	轻度组 (n=177)	中重度组 (n=145)	t/Z 值	P 值
hsCRP(mg/L)[a]	28.0±16.6	30.1±17.2	1.231	0.268
sdLDL-C(mmol/L)[b]	1.0 (0.5, 1.3)	1.0 (0.4, 1.5)	0.001	0.989
HbA1c(%)[a]	8.2±2.6	7.8±2.3	1.697	0.194
TC(mmol/L)[b]	5.3 (4.3, 6.8)	5.9 (4.5, 7.7)	5.021	0.025
TG(mmol/L)[b]	2.6 (1.4, 3.7)	2.6 (1.4, 4.0)	0.209	0.648
HDL-C(mmol/L)[b]	1.9 (1.4, 2.5)	1.7 (1.3, 2.4)	1.432	0.231
LDL-C(mmol/L)[b]	2.2 (1.2, 3.4)	2.3 (1.0, 3.2)	0.651	0.420
Lp(a)(mg/L)[b]	263.2 (161.3, 346.2)	451.6 (284.7, 543.8)	85.147	<0.001
FPG(mmol/L)[a]	10.4±3.6	11.3±3.3	4.947	0.027
RC(mmol/L)[a]	1.4±0.6	1.7±0.6	13.372	<0.001
TyG[a]	9.6±1.0	9.8±0.9	1.607	0.206

注：[a] 表示数据为 $\bar{x}\pm s$；[b] 表示数据为 $M(Q_1, Q_3)$。

表 3　T2DM 患者冠状动脉病变严重程度的影响因素

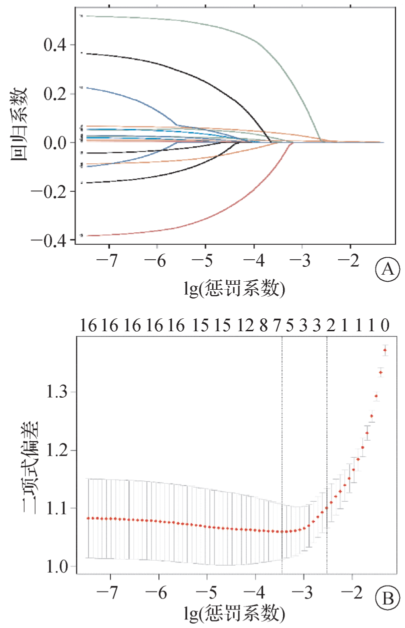
Tab. 3　Factors influencing the severity of coronary artery lesions in patients with T2DM

变量	回归系数	标准误	Wald 值	P 值	OR 值	95%CI
年龄	0.061	0.019	10.773	0.001	1.063	1.025～1.102
FPG	0.061	0.041	2.186	0.139	1.063	0.980～1.152
TC	0.036	0.080	0.201	0.654	1.037	0.886～1.213
Lp(a)	0.009	0.001	62.437	<0.001	1.009	1.007～1.012
RC	0.574	0.264	4.724	0.030	1.775	1.058～2.977

表 4　T2DM 患者冠状动脉病变严重程度的最佳预测因素

Tab. 4　Best predictors of coronary artery lesions severity in patients with T2DM

变量	估计值	标准差	Z 值	P 值
年龄	0.061	0.019	3.251	0.001
FPG	0.069	0.042	1.659	0.097
TC	−0.432	0.225	−1.917	0.055
Lp(a)	0.009	0.001	7.989	<0.001
RC	0.631	0.246	2.565	0.010



注：A 为回归系数分布剖面图；B 为最优的惩罚系数(λ 值)。

图 1　LASSO 回归筛选 T2DM 患者冠状动脉病变严重程度的最佳预测因素

Fig. 1　LASSO regression screening of the best predictors of coronary artery lesions severity in T2DM patients

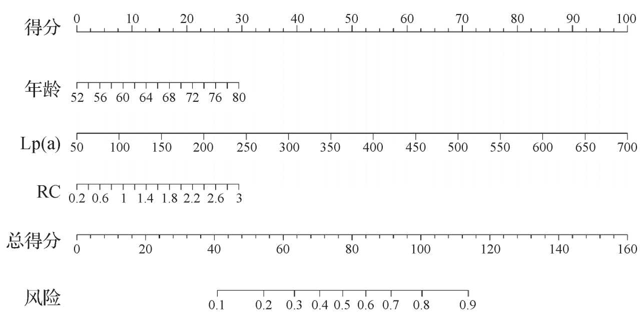


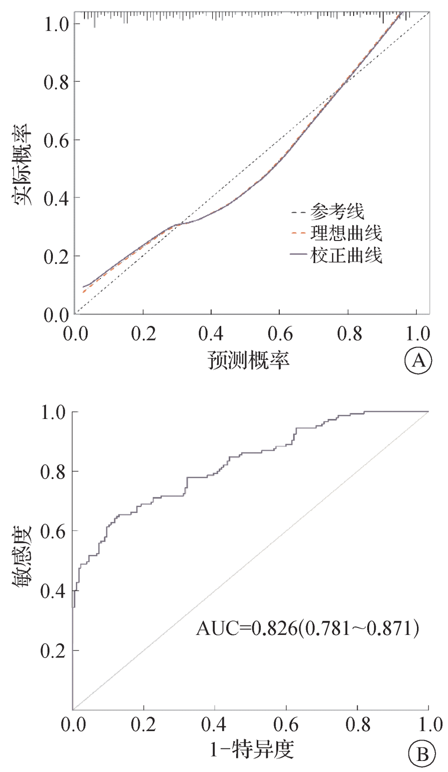
图 2　T2DM 患者冠状动脉病变严重程度的预测模型列线图

Fig. 2　Nomogram of the predictive model of coronary artery lesions severity in patients with T2DM

表 5　预测因素赋分公式

Fig. 5　Grading formula of the predictors

变量	赋分公式
年龄赋分	1.050 198 137×年龄值−54.610 303 105
Lp(a)赋分	0.153 846 154×Lp(a)值−7.692 307 692
RC 赋分	10.508 359 349×RC 值−2.101 671 870



注:A 为预测模型校准曲线;B 为预测模型 ROC 曲线。

图 3　列线图模型的准确性评价

Fig. 3　Accuracy evaluation of the nomogram prediction model

3 讨　论

与健康人群相比,高血压、肥胖、血脂异常等病理状态在 T2DM 患者中更为常见,上述因素也是 CAD 的危险因素[8]。在循环系统中,内皮型一氧化氮合酶参与血管功能的调节,其产生的一氧化氮是内皮依赖性松弛相关的关键血管活性因子,高血糖状态可减少内皮型一氧化氮合酶的合成,降低一氧化氮的生物利用度,导致内皮功能障碍[9]。高血糖和游离脂肪酸可上调血管内皮细胞微小 RNA-34a 的表达水平,靶向沉默信息调节因子 1,抑制 P53 基因乙酰化,增强 P53 基因及下游衰老相关基因转录活性,导致内皮细胞衰老,引起内皮功能障碍,加速动脉粥样硬化进程[10-11]。高血糖状态下,机体晚期糖基化终末产物积累,通过与受体相互作用,晚期糖基化终末产物可通过改变细胞活性、促进基因表达、增加炎症化合物的流出等途径,诱导动脉壁损伤和斑块形成,加速动脉粥样硬化的发展[12]。此外,高血糖状态可改变冠状动脉的结构和功能。研究表明,T2DM 患者冠状动脉小分支内皮细胞和内皮下细胞增生,且合并纤维化[13]。

T2DM 患者多合并脂质代谢异常,脂质代谢异常也是 CAD 的危险因素之一,积极干预血脂异常等 CAD 危险因素可降低 T2DM 患者心血管事件的发生率[14]。Lp(a)主要由低密度脂蛋白样颗粒与载脂蛋白 A、载脂蛋白 B 复合而成,其内部游离脂肪酸含量较高,更易被氧化,氧化型 Lp(a)也更易作用于动脉内皮细胞,诱导内皮细胞损伤[15-16]。内皮细胞在氧化型 Lp(a)的刺激下会释放细胞因子生长因子,诱导单核细胞向内皮细胞黏附聚集及跨内皮转运,吞噬进入内膜的脂质,最终演化为泡沫细胞[17]。本研究结果表明, Lp(a)水平与 T2DM 患者中重度冠状动脉病变密切相关,在校正了年龄、RC 等因素的干扰后,高水平的 Lp(a)仍是 T2DM 患者中重度冠状动脉病变的独立预测因子,且准确性较好。

年龄与冠状动脉病变严重程度及预后的相关性已得到证实[18]。有研究表明,老年 T2DM 合并 CAD 患者(>60 岁)冠状动脉病变以三支病变和弥漫性病变为主,病情更为复杂严重[19]。本研究也证实了年龄是 T2DM 合并 CAD 严重程度的独立预测因子,且预测准确性较好。

前期研究证实,RC 水平升高与动脉粥样硬化呈正相关[20],RC 也是心血管疾病的有效预测因子[21]。Castañer 等[22]组织实施的 PREDIMED 研究发现,RC 水平每升高 10 mg/dL,主要心血管不良事件的发生风险增加 21%,当 RC>30 mg/dL 时,患者主要心血管不良事件的风险均高于 RC≤30 mg/dL 者,且该预测结果不受 LDL-C 水平的影响。Quispe 等[23]的研究发现,RC 与心血管疾病存在正相关性,RC 可作为独立于 LDL-C、载脂蛋白 B 等因素之外的危险因素,预测急性 CAD 的发病风险。

本研究结果表明,年龄大、RC 和 Lp(a)水平高是 T2DM 患者中重度冠状动脉病变的独立预测因子,上述因子联合预测 T2DM 患者冠状动脉病变严重程度的准确性较好。但由于本研究纳入的样本量较少,且为回顾性分析,年龄、RC 和 Lp(a)水平与 T2DM 患者冠状动脉病变严重程度的相关性及预测价值仍需更大样本量或前瞻性研究进一步证实。

利益冲突　无

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