·临床研究·

年龄、肌酐和射血分数Ⅱ评分,血清视黄醇结合蛋白4及氨基末端B型利钠肽前体水平对老年急性冠脉综合征合并2型糖尿病患者经皮冠状动脉介入治疗术后的预后评估价值

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【摘 要】 目的 探讨年龄、肌酐和射血分数(ACEF)Ⅱ评分,血清视黄醇结合蛋白4(RBP4)及氨基末端B型利钠肽前体(NT-proBNP)水平对老年急性冠脉综合征(ACS)合并2型糖尿病(T2DM)患者经皮冠状动脉介入治疗(PCI)术后的预后评估价值。**方法** 收集2022年1月至2023年9月邢台市中心医院收治的128例行PCI治疗的老年ACS合并T2DM患者的临床资料。根据患者预后是否出现主要不良心脑血管事件,分为预后良好组(99例)与预后不良组(29例)。采用SPSS 24.0统计软件进行数据分析。根据数据类型,组间比较分别采用*t*检验、Mann-Whitney *U*检验、χ^2检验或Fisher精确概率法。采用受试者工作特征(ROC)曲线评估ACEFⅡ评分及血清RBP4、NT-proBNP水平对患者PCI术后预后不良的预测价值。采用二元logistic回归分析评估患者PCI术后预后的影响因素。**结果** 128例老年ACS合并T2DM患者中,PCI术后6个月有29例(22.66%)出现主要不良心脑血管事件,包括7例心力衰竭、5例卒中、7例心肌梗死、9例二次血运重建及1例心源性死亡。预后不良组术后达格列净用药率显著低于预后良好组,ACEFⅡ评分及血清RBP4、NT-proBNP水平均显著高于预后良好组,差异均有统计学意义(均$P<0.05$)。ROC曲线分析显示,ACEFⅡ评分及血清RBP4、NT-proBNP水平预测老年ACS合并T2DM患者PCI术后预后不良的曲线下面积(AUC)分别为0.745(95%*CI* 0.640~0.850;$P<0.05$)、0.871(95%*CI* 0.803~0.939;$P<0.05$)、0.796(95%*CI* 0.697~0.902;$P<0.05$)。二元logistic回归分析显示,ACEFⅡ评分≥1.59分(*OR*=3.357,95%*CI* 1.688~6.676;$P<0.05$)、RBP4≥42.71 mg/L(*OR*=3.873,95%*CI* 2.206~6.800;$P<0.05$)、NT-proBNP≥603.58 ng/L(*OR*=3.725,95%*CI* 2.114~6.562;$P<0.05$)均为老年ACS合并T2DM患者PCI术后预后不良的独立危险因素,术后应用达格列净则为独立保护因素(*OR*=0.380,95%*CI* 0.011~0.782;$P<0.05$)。**结论** ACEFⅡ评分与血清RBP4、NT-proBNP水平在辅助预测老年ACS合并T2DM患者PCI术后预后中具有一定作用,术后使用达格列净降糖可能对改善患者预后有利。

【关键词】 老年人;年龄、肌酐和射血分数Ⅱ评分;视黄醇结合蛋白4;氨基末端B型利钠肽前体;急性冠脉综合征;2型糖尿病
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Predictive value of ACEF Ⅱ score and serum RBP4 and NT-proBNP levels for prognosis of elderly T2DM patients with acute coronary syndrome after PCI

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【Abstract】 Objective To explore the predictive value of age, creatinine and ejection fraction (ACEF) Ⅱ score, and serum retinol binding protein 4 (RBP4) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels for the prognosis in elderly patients with type 2 diabetes mellitus (T2DM) complicated with acute coronary syndrome (ACS) after percutaneous coronary intervention (PCI). **Methods** Clinical data of 128 elderly T2DM patients with ACS undergoing PCI in our hospital from January 2022 to September 2023 were collected. According to whether major adverse cardiovascular and cerebrovascular events occurred, they were divided into good prognosis group (99 cases) and poor prognosis group (29 cases). SPSS statistics 24.0 was used for data analysis. Depending on data type, *t* test, Mann-Whitney *U* test, χ^2 test or Fisher's exact probability test was applied for comparison between groups. Receiver operating characteristic (ROC) curve was plotted to evaluate the predictive value of ACEF Ⅱ score and serum RBP4 and NT-proBNP levels for poor prognosis, and binary logistic regression analysis was used to determine the influencing factors of prognosis in these patients after PCI. **Results** Among the 128 elderly T2DM patients with ACS, 29 (22.66%) had major adverse cardiovascular and cerebrovascular

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events at 6 months after PCI, including 7 cases of heart failure, 5 cases of stroke, 7 cases of myocardial infarction, 9 cases of secondary revascularization, and 1 case of cardiac death. The poor prognosis group demonstrated significantly lower postoperative administration rate of dapagliflozin, but higher ACEF Ⅱ score and serum levels RBP4 and NT-proBNP than the good prognosis group (all $P<0.05$). ROC curve analysis showed that the areas under the curve (AUC) of ACEF Ⅱ score and serum RBP4 and NT-proBNP levels in predicting poor prognosis after PCI in elderly T2DM patients with ACS was 0.745 (95%*CI* 0.640-0.850, $P<0.05$), 0.871 (95%*CI* 0.803-0.939, $P<0.05$) and 0.796 (95%*CI* 0.697-0.902, $P<0.05$), respectively. Binary logistic regression analysis suggested that ACEF Ⅱ score ≥ 1.59 (*OR*=3.357, 95%*CI* 1.688-6.676, $P<0.05$), RBP4 ≥42.71 mg/L (*OR*=3.873, 95%*CI* 2.206-6.800, $P<0.05$), and NT-proBNP≥603.58 ng/L (*OR*=3.725, 95%*CI* 2.114-6.562, $P<0.05$) were all independent risk factors for poor prognosis in elderly T2DM patients with ACS after PCI, and postoperative use of dapagliflozin (*OR*=0.380, 95%*CI* 0.011-0.782, $P<0.05$) was an independent protective factor. **Conclusion** ACEF Ⅱ score, serum RBP4 and NT-proBNP levels can play a certain role in predicting the prognosis of elderly T2DM patients with ACS after PCI, and the postoperative use of dapagliflozin may be beneficial to improving the prognosis of the patients.

【Key words】 aged; age, creatinine and ejection fraction Ⅱ score; retinol binding protein 4; N-terminal pro-B-type natriuretic peptide; acute coronary syndrome; type 2 diabetes mellitus

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冠心病是威胁我国老年人群生命健康的主要疾病之一,随着老龄化现象的加剧,冠心病患病人群显著增多,其中急性冠脉综合征(acute coronary syndrome, ACS)疾病进展快,需及时入院治疗[1]。2型糖尿病(type 2 diabetes mellitus, T2DM)作为危害全球公共健康的重要疾病,也是心血管疾病不良预后的高危因素,老年冠心病合并T2DM患者在临床并不少见,较无T2DM的老年冠心病患者预后更差[2]。经皮冠状动脉介入术(percutaneous coronary intervention, PCI)已成为临床广泛应用的微创疗法,在降低ACS患者致残率及致死率方面具有优势,但部分患者PCI术后仍出现预后不良,如何预测PCI术后预后状况是近年研究的热点与难点[3]。年龄、肌酐和射血分数(age, creatinine and ejection fraction, ACEF)Ⅱ评分是在原ACEF评分的基础上优化改进的新工具,可用于评估ACS患者术后死亡风险[4]。视黄醇结合蛋白4(retinol binding protein 4, RBP4)是一种新型脂肪因子,能通过诱导炎症反应,加剧内皮细胞损伤,近年被发现不仅参与T2DM患者血管并发症的发生机制,也促进ACS的进展[5]。氨基末端B型利钠肽前体(N-terminal pro-B-type natriuretic peptide, NT-proBNP)是心力衰竭的重要标志物,近年也被用于ACS患者预后预测[6]。基于此,本研究分析ACEF Ⅱ评分及血清RBP4、NT-proBNP在老年ACS合并T2DM患者预后评估中的应用价值,以期为疾病临床管理工作提供参考数据。

1 对象与方法

1.1 研究对象

回顾性分析2022年1月至2023年9月邢台市中心医院收治的128例行PCI治疗的老年ACS合并T2DM患者的临床资料。纳入标准:符合《急性冠脉综合征临床实践指南》[7]中ACS诊断标准;符合《中国2型糖尿病防治指南(2020年版)》[8]中T2DM诊断标准;发病12 h内入院行PCI治疗,且治疗符合《中国经皮冠状动脉介入治疗指南(2016)》[9];PCI术后临床试验血流分级[10]为3级,血流灌注正常;首次接受PCI治疗;年龄≥60岁;PCI术后随访时间≥6个月;实验室检查、影像学检查等资料完整。排除标准:入院前接受达格列净降糖治疗;合并甲亢等甲状腺疾病或自身免疫性疾病;存在急慢性感染或传染病;合并T2DM急性或慢性并发症,如酮症酸中毒、糖尿病视网膜病变等;合并先天性心脏病等其他心脏器质性病变;存在帕金森等神经系统疾病或阿尔兹海默症等认知功能障碍;血液系统疾病;恶性肿瘤;PCI术后6个月内发生车祸伤等意外事件。

1.2 方法

1.2.1 临床资料收集 所有患者在入院2 h内采集外周肘静脉血3~4 ml,经3 000转/min离心10 min(半径8 cm),得到血清标本。采用化学发光法(德国Roche公司)检测血清RBP4、NT-proBNP水平;采用全自动生化分析仪(中国迈瑞公司,型号:BS-350S)检测血肌酐,全自动血细胞分析仪(日本Sysmex公司,型号:XN-20)检测红细胞压积;采用彩色多普勒超声仪(美国General Electric公司,型号:LOGIQ9)检测左室射血分数;根据Ranucci等[11]提出的ACEF Ⅱ计算公式计算评分,ACEF Ⅱ评分=年龄(岁)/左室射血分数(%)+2.0(血肌酐>176.8 μmol/L时)+3.0(急诊手术时)+0.2×(36%-红细胞压积),红细胞压积<36%时取实测值,≥36%时取36%代入计算;其他既往史、术后用药等情况均经电子病历获得。

1.2.2 PCI治疗 两组患者均采用右侧桡动脉入路Judkins法行冠状动脉造影,确定靶血管,在导丝通过及球囊扩张见明显血栓时实施血栓抽吸。PCI术前给予阿司匹林肠溶片300 mg/d,术后改为100 mg/d,口服;术前替格瑞洛片180 mg/次,术后改

为 90 mg/次,2 次/d,口服。术后常规使用 β 受体阻滞剂等药物治疗。PCI 术后临床试验血流分级[10]为 3 级,血流灌注正常。

1.2.3 预后评估 参考美国心脏协会临床实践指南联合委员会 2021 年提出的指南意见[12],记录 PCI 术后 6 个月内出现的不良心脑血管事件,包括心力衰竭、卒中、心肌梗死、二次血运重建、心源性死亡等。根据预后是否出现主要不良心脑血管事件,分为预后良好组(99 例)与预后不良组(29 例)。

1.3 统计学处理

采用 SPSS 24.0 统计软件进行数据分析。计量资料呈正态分布者以均数±标准差($\bar{x}\pm s$)表示,组间比较采用 t 检验;呈非正态分布者以中位数(四分位数间距)[$M(Q_1, Q_3)$]表示,组间比较采用 Mann-Whitney U 检验。计数资料以例数(百分率)表示,组间比较采用 χ^2 检验或 Fisher 精确概率法。采用受试者工作特征(receiver operating characteristic, ROC)曲线评估 ACEF Ⅱ 评分及血清 RBP4、NT-proBNP 对老年 ACS 并 T2DM 患者 PCI 术后预后不良的预测价值,记录曲线下面积(area under the curve, AUC)。采用 logistic 回归模型分析 ACS 合并 T2DM 患者 PCI 术后预后不良的影响因素。$P<0.05$ 为差异有统计学意义。

2 结 果

2.1 患者预后情况

128 例老年 ACS 合并 T2DM 患者中,PCI 术后 6 个月有 29 例(22.66%)出现主要不良心脑血管事件,包括 7 例心力衰竭、5 例卒中、7 例心肌梗死、9 例二次血运重建、1 例心源性死亡。

2.2 两组患者一般资料

预后不良组患者术后达格列净用药率显著低于预后良好组,ACEF Ⅱ 评分及血清 RBP4、NT-proBNP 水平均显著高于预后良好组,差异均有统计学意义($P<0.05$;表 1)。

表 1 两组患者一般资料比较

Table 1 Comparison of general data between two groups

Item	Poor prognosis group ($n=29$)	Good prognosis group ($n=99$)	$\chi^2/t/Z$	P value
Gender[n(%)]			0.053	0.818
Male	22(75.86)	73(73.74)		
Female	7(24.14)	26(26.26)		
Age(years, $\bar{x}\pm s$)	68.89±4.81	68.24±4.56	0.667	0.506
Body mass index(kg/m^2, $\bar{x}\pm s$)	23.25±2.30	23.54±2.19	0.620	0.536
Hypertension[n(%)]	18(62.07)	59(59.60)	0.057	0.811
Hyperlipidemia[n(%)]	3(10.34)	8(8.08)	0.146	0.702
Smoking history[n(%)]	15(51.72)	52(52.53)	0.006	0.939
Drinking history[n(%)]	6(20.69)	13(13.13)	1.014	0.314
T2DM course(years, $\bar{x}\pm s$)	11.64±2.12	10.95±2.04	1.588	0.115
Type of acute coronary syndrome[n(%)]			0.152	0.927
ST elevation myocardial infarction	21(72.41)	69(69.70)		
Non-ST elevation myocardial infarction	6(20.69)	21(21.21)		
Angina pectoris	2(6.90)	9(9.09)		
Serum creatinine(μmol/L, $\bar{x}\pm s$)	6.12±1.24	5.78±1.08	1.441	0.152
Hematocrit(%, $\bar{x}\pm s$)	39.63±3.55	40.24±4.02	0.737	0.463
Cardiactroponin I(ng/ml, $\bar{x}\pm s$)	6.35±1.27	5.89±1.54	1.468	0.145
Creatine kinase isoenzyme(ng/ml, $\bar{x}\pm s$)	8.36±1.62	7.89±1.48	1.472	0.144
Hemoglobin(g/L, $\bar{x}\pm s$)	132.46±10.47	136.27±11.19	1.635	0.105
Fasting blood glucose(mmol/L, $\bar{x}\pm s$)	8.14±1.25	7.93±1.33	0.758	0.450
Glycosylated hemoglobin(%, $\bar{x}\pm s$)	8.78±0.98	8.45±1.12	1.433	0.154
Left ventricular ejection fraction(%, $\bar{x}\pm s$)	55.49±4.69	57.22±5.12	1.630	0.106
ACEF Ⅱ score(points, $\bar{x}\pm s$)	1.56±0.29	1.31±0.17	5.889	<0.001
RBP4(mg/L, $\bar{x}\pm s$)	49.88±7.43	38.81±6.71	7.619	<0.001
NT-proBNP[ng/L, $M(Q_1, Q_3)$]	656.61(590.70,735.13)	553.28(489.15,606.80)	4.215	<0.001
Responsible vessel[n(%)]			0.086	0.958
Anterior descending branch	15(51.72)	54(54.55)		
Right coronary artery	11(37.93)	36(36.36)		
Left circumflex branch	3(10.34)	9(9.09)		
Number of implanted stents(piece, $\bar{x}\pm s$)	1.42±0.29	1.35±0.28	1.175	0.242
Postoperative medication[n(%)]				
Metformin	29(100.00)	99(100.00)	*	1.000
Insulin aspart	15(51.72)	44(44.44)	0.478	0.489
Dapagliflozin	3(10.34)	35(35.35)	6.721	0.010
β-blocker	25(86.21)	82(82.83)	0.187	0.666
Angiotensin converting enzyme inhibitor/angiotensin Ⅱ receptor antagonist	22(75.86)	71(71.72)	0.194	0.660
Statins	28(96.55)	96(96.97)	0.013	0.909
Nitrates	3(10.34)	8(8.08)	0.146	0.702

T2DM: type 2 diabetes mellitus; ACEF Ⅱ: age, creatinine and ejection fraction Ⅱ; RBP4: retinol binding protein 4; NT-proBNP: N-terminal pro-B-type natriuretic peptide. *: Fisher's exact probability test.

2.3 ACEFⅡ评分及血清RBP4、NT-proBNP对患者预后不良的预测价值

ROC曲线分析显示，ACEFⅡ评分及血清RBP4、NT-proBNP预测老年ACS并T2DM患者PCI术后预后不良的AUC值分别为0.745、0.871、0.796（均P<0.05；表2、图1）。

表2 ACEFⅡ评分及血清RBP4、NT-proBNP对老年ACS并T2DM患者PCI术后预后不良的预测价值

Table 2 Predictive value of ACEFⅡ score, serum RBP4 and NT-proBNP on poor prognosis after PCI in elderly patients with ACS and T2DM

Indicator	Cut-off value	Sensitivity (%)	Specificity (%)	AUC	95%*CI*	*P* value
ACEFⅡ score	1.59 points	41.38	95.96	0.745	0.640–0.850	<0.001
RBP4	42.71 mg/L	86.21	76.77	0.871	0.803–0.939	<0.001
NT-proBNP	603.58 ng/L	79.31	73.74	0.796	0.697–0.902	<0.001

ACEFⅡ: age, creatinine and ejection fraction Ⅱ; RBP4: retinol binding protein 4; NT-proBNP: N-terminal pro-B-type natriuretic peptide; ACS: acute coronary syndrome; T2DM: type 2 diabetes mellitus; PCI: percutaneous coronary intervention; AUC: area under the curve.

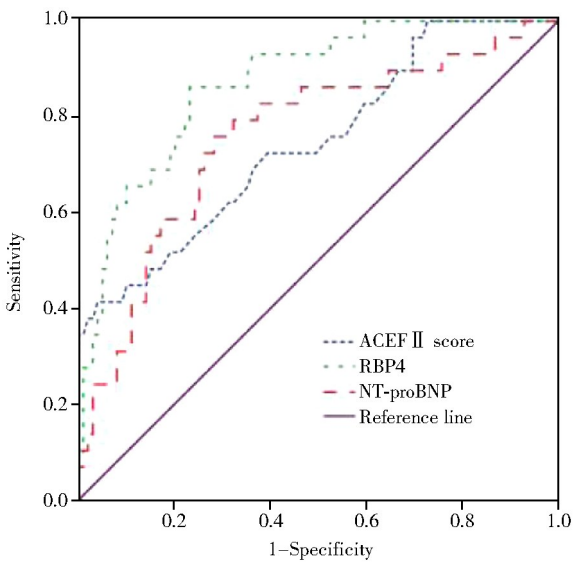


图1 ACEFⅡ评分及血清RBP4、NT-proBNP预测老年ACS合并T2DM患者PCI术后预后不良的ROC曲线

Figure 1 ROC curves of ACEFⅡ score, serum RBP4 and NT-proBNP in predicting poor prognosis after PCI in elderly patients with ACS and T2DM

ACEFⅡ: age, creatinine and ejection fraction Ⅱ; RBP4: retinol binding protein 4; NT-proBNP: N-terminal pro-B-type natriuretic peptid; ACS: acute coronary syndrome; T2DM: type 2 diabetes mellitus; PCI: percutaneous coronary intervention; ROC: receiver operating characteristic.

2.4 老年ACS合并T2DM患者PCI术后预后不良的影响因素

将表1中有统计学意义的指标赋值代入二元logistic回归分析，结果显示ACEFⅡ评分≥1.59分、RBP4≥42.71 mg/L、NT-proBNP≥603.58 ng/L均为老年ACS合并T2DM患者PCI术后预后不良的独立危险因素，术后应用达格列净则为独立保护因素（均P<0.05；表3）。

表3 老年ACS合并T2DM患者PCI术后预后不良的二元logistic回归分析

Table 3 Binary logistic regression analysis of poor prognosis after PCI in elderly patients with ACS and T2DM

Factor	β	*SE*	*Wald* χ^2	*P* value	*OR*	95%*CI*
ACEFⅡ score ≥ 1.59 points	1.211	0.421	8.274	0.004	3.357	1.688–6.676
RBP4≥42.71 mg/L	1.354	0.398	11.574	0.001	3.873	2.206–6.800
NT-proBNP≥603.58 ng/L	1.315	0.389	11.428	0.001	3.725	2.114–6.562
Postoperative use of dapagliflozin	−0.968	0.289	11.219	0.001	0.380	0.011–0.782

ACS: acute coronary syndrome; T2DM: type 2 diabetes mellitus; PCI: percutaneous coronary intervention; ACEFⅡ: age, creatinine and ejection fraction Ⅱ; RBP4: retinol binding protein 4; NT-proBNP: N-terminal pro-B-type natriuretic peptide.

3 讨 论

T2DM及ACS均以老年人为好发人群，两者共病在老年患者中较为常见，高血糖可增加血管内皮损伤，导致ACS患者心血管事件风险升高，增加患者预后死亡率，故老年ACS合并T2DM患者的预后受到临床的广泛关注[13]。PCI治疗虽然能降低ACS患者致残率及致死率，但仍有部分患者出现预后不良，目前仍缺乏行之有效的PCI术后预后不良预测工具，导致临床管理难度较大[14]。因此，本研究就老年ACS合并T2DM患者PCI术后预后不良状况及其高危因素展开分析，以期为其临床管理提供可靠数据。本研究中，128例老年患者术后6个月不良事件发生率为22.66%，与国内报道的18.89%结果相近[14]。

ACEFⅡ评分是在年龄、肾功能及心功能的基础上，结合贫血程度及入院病情轻重急缓的综合评估工具，被认为是评估PCI手术风险的有效工具[15]。本研究发现，ACEFⅡ评分对预测老年ACS合并T2DM患者PCI术后预后不良的AUC高达0.745（P<0.05），且ACEFⅡ评分≥1.59分为老年ACS合并T2DM患者PCI术后预后不良的独立危险因素，提示ACEFⅡ评分可预测患者预后状况。究其原因可能为术前年龄更高、肾功能及心功能更差、贫血更严重的急诊ACS患者经PCI手术获益更困难，术后风险事件更多。RBP4是新发现的参与炎症反应的脂肪因子，可通过激活Toll样受体4等信号通路，促进炎症

因子增多,诱导内皮细胞炎症,加速动脉粥样硬化进程,在 ACS 进程及 T2DM 血管病变中均能发挥促进作用[16]。本研究结果显示,血清 RBP4 对预测老年 ACS 并 T2DM 患者 PCI 术后预后不良的 AUC 高达 0.871(P<0.05),且 RBP4≥42.71 mg/L 为老年 ACS 并 T2DM 患者 PCI 术后预后不良的独立危险因素,提示检测 RBP4 有望成为独立预测因子,辅助临床判断患者预后。该结果可能与术前血管内皮炎症越严重的患者 PCI 术后更易出现再栓塞等不良事件、且预后更差有关。NT-proBNP 可反映心室超负荷及心室容积扩大,不仅能用于诊断心力衰竭,也能评估心室重构程度,预测 ACS 患者预后[17]。本研究中,NT-proBNP 对预测老年 ACS 合并 T2DM 患者 PCI 术后预后不良的 AUC 达 0.796(P<0.05),且 NT-proBNP≥603.58 ng/L 是预后不良的独立危险因素,提示 NT-proBNP 作为常用的心力衰竭评估工具,也可能作为独立预测因子,在老年 ACS 合并 T2DM 预后评估中发挥积极作用。分析其原因为 NT-proBNP 水平越高,提示患者心室重构程度越严重,心脏结构发生显著改变,此类患者 PCI 术后心功能更难得到有效逆转,进而导致预后不良。

据文献报道[18],达格列净的渗透性利尿作用可减轻心脏前负荷,且具有一定抗心肌细胞纤维化作用,可使 T2DM 患者心血管获益,是一种安全有效的新型降糖药。本研究也发现,术后应用达格列净是老年 ACS 合并 T2DM 患者 PCI 术后预后不良的独立保护因素,提示达格列净可能促进老年 ACS 合并 T2DM 患者 PCI 术后心脏负荷减轻,使患者心血管获益,值得临床关注。但由于相关报道少见,达格列净对 PCI 术后预后的保护作用机制还需更多临床试验的进一步探究。

综上,ACEFⅡ评分及血清 RBP4、NT-proBNP 有望成为新的独立预测因子,辅助临床评估老年 ACS 合并 T2DM 患者 PCI 术后的预后状况,且术后应用达格列净降糖可能对改善患者预后有积极作用。然而,由于本研究样本量较小,且为单中心研究,存在代表性欠缺等缺陷,上述结论还需后续大样本量多中心研究的验证。

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