

甘油三酯葡萄糖指数与冠心病患者经皮冠状动脉介入术后发生支架内再狭窄的关联性研究

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[摘要] 目的 探讨甘油三酯葡萄糖(TyG)指数与冠心病患者经皮冠状动脉介入(PCI)术后发生支架内再狭窄(ISR)的关联性。方法 通过医院电子病历系统收集2016年1月至2021年9月昆明医科大学第二附属医院心内科收治的243例冠心病患者的临床资料，其中男179例，女64例，年龄(60.92 ± 11.13)岁，均行PCI治疗并完成术后随访。根据随访期间发生ISR情况将其分为ISR组(45例)和非ISR组(198例)。比较两组的一般临床资料、手术相关指标及PCI术前和术后的生化指标。通过二元logistic回归分析影响冠心病患者PCI术后发生ISR的危险因素。结果 ISR组吸烟、合并糖尿病人数比例高于非ISR组，差异有统计学意义($P < 0.05$)。两组在年龄、性别、合并高血压病、体质质量指数(BMI)、Gensini评分、支架植入总数、植入支架直径、植入支架长度、多支血管病变、弥漫性病变等方面比较差异均无统计学意义($P > 0.05$)。在术前，ISR组的TC、TG、FBG和TyG指数水平高于非ISR组，差异有统计学意义($P < 0.05$)。在复查造影时，ISR组TyG指数水平和TyG指数未达标人数比例大于非ISR组，差异有统计学意义($P < 0.05$)。二元logistic回归分析结果显示，吸烟($OR = 6.592$)、合并糖尿病($OR = 3.843$)、复查时TyG指数未达标($OR = 23.273$)是冠心病患者PCI术后发生ISR的独立危险因素($P < 0.05$)。结论 TyG指数升高会增加冠心病患者PCI术后发生ISR的风险，PCI术后应加强患者控制TyG指数的管理。

[关键词] 经皮冠状动脉介入；支架内再狭窄；甘油三酯葡萄糖指数

[中图分类号] R 543.3 **[文献标识码]** A **[文章编号]** 1674-3806(2022)07-0631-05

doi:10.3969/j.issn.1674-3806.2022.07.14

A study on association between triglyceride-glucose index and in-stent restenosis after percutaneous coronary intervention in patients with coronary heart disease CHEN Ling-ling, LI Bo. Department of Cardiology, the Second Affiliated Hospital of Kunming Medical University, Yunnan 650101, China

[Abstract] **Objective** To investigate the association between triglyceride-glucose(TyG) index and in-stent restenosis(ISR) after percutaneous coronary intervention(PCI) in patients with coronary heart disease. **Methods** The clinical data of 243 patients with coronary heart disease who were admitted to Department of Cardiology, the Second Affiliated Hospital of Kunming Medical University from January 2016 to September 2021 were collected through the hospital electronic medical record system, including 179 males and 64 females, with an average age of (60.92 ± 11.13)years. All the patients underwent percutaneous coronary intervention(PCI) and their postoperative follow-up was completed. According to the occurrence of in-stent restenosis(ISR) during the follow-up period, the patients were divided into ISR group(45 cases) and non-ISR group(198 cases). The general clinical data, operation-related indexes, and biochemical indexes before and after PCI were compared between the two groups. The risk factors of ISR after PCI in patients with coronary heart disease were analyzed by binary logistic regression. **Results** The proportion of smoking patients and diabetes patients in the ISR group was higher than that in the non-ISR group, and the difference was statistically significant($P < 0.05$). There were no statistically significant differences between the two groups in age, gender, complicated hypertension, body mass index(BMI), Gensini score, total number of implanted stents, diameter of implanted stents, length of implanted stents, multivessel disease, and diffuse disease($P > 0.05$). Before operation, the levels of total cholesterol(TC), triglyceride(TG), fasting blood glucose(FBG) and TyG indexes in the ISR group were higher than those in the non-ISR

group, and the differences were statistically significant ($P < 0.05$). During the re-examination of angiography, the level of TyG index and the proportion of the patients who did not meet the standard of TyG index in the ISR group were greater than those in the non-ISR group, and the differences were statistically significant ($P < 0.05$). The results of binary logistic regression analysis showed that smoking ($OR = 6.592$), complicated diabetes mellitus ($OR = 3.843$), and substandard TyG index at re-examination ($OR = 23.273$) were the independent risk factors for ISR after PCI in the patients with coronary heart disease ($P < 0.05$). **Conclusion** Elevated TyG index may increase the risk of ISR in patients with coronary heart disease after PCI, and the management of TyG index control should be strengthened in the patients after PCI.

[Key words] Percutaneous coronary intervention(PCI); In-stent restenosis(ISR); Triglyceride-glucose(TyG) index

冠状动脉粥样硬化性心脏病(简称冠心病)是严重威胁人类健康的主要疾病之一,其发病率和病死率逐年递增。经皮冠状动脉介入(percutaneous coronary intervention,PCI)是冠心病患者血运重建的主要治疗方法^[1],但术后仍有部分患者出现支架内再狭窄(in-stent restenosis,ISR),易出现不稳定型心绞痛症状和不良心血管事件^[2],严重影响患者的生活质量,是一个亟需攻克的临床难题。胰岛素抵抗是细胞对正常浓度胰岛素的生理反应欠佳^[3],是以葡萄糖摄取和利用效率低下为特征的病理状态。胰岛素抵抗不仅是糖尿病的主要发病机制,也是心血管疾病发生和不良预后的重要危险因素。有研究发现,发生ISR患者的胰岛素抵抗水平增加,而甘油三酯葡萄糖(triglyceride-glucose,TyG)指数被建议作为胰岛素抵抗的替代标志物,其升高与心血管疾病风险增加有关^[4]。本研究旨在探讨TyG水平对冠心病患者PCI治疗后发生ISR的影响,现报道如下。

1 资料与方法

1.1 临床资料 通过医院电子病历系统收集2016年1月至2021年9月昆明医科大学第二附属医院心内科收治的243例冠心病患者的临床资料,其中男179例,女64例,年龄(60.92 ± 11.13)岁,均行PCI治疗并完成术后6~12个月随访。纳入标准:(1)首次确诊冠心病;(2)行PCI治疗,植入雷帕霉素药物洗脱支架;(3)依从性良好,完成术后6~12个月的随访;(4)支架植入后规律行双联抗血小板聚集治疗,并予他汀类药物等进行冠心病二级预防。排除标准:(1)年龄<18岁;(2)首次PCI于外院完成;(3)有冠状动脉瘤、冠状动脉夹层或既往冠状动脉旁路移植病史;(4)有心力衰竭、心脏瓣膜病和先天性心脏病病史;(5)合并严重肾脏疾病、肝脏疾病以及血液系统、免疫系统和肿瘤相关疾病。

1.2 手术方法 采用德国西门子DSA造影系统,以Seldinger's改良法穿刺桡动脉或股动脉,采用标准Judkin's法多角度多体位作选择性左右冠脉造影。植

入支架均为雷帕霉素洗脱支架。术后予规范的二级预防方案治疗,包括规律服用双联抗血小板聚集治疗、他汀类药物治疗。由两位心内科介入医师评估冠脉病变情况,完善造影报告,记录病变血管的狭窄程度。当出现评估结果不一致时则由第三位同级别医师进一步分析和评价。

1.3 随访 嘱患者术后6~12个月返院复查血生化等血清学指标和冠状动脉造影。ISR影像学诊断标准^[5]:冠状动脉造影显示支架段内或支架近段或支架远端5 mm以内存在狭窄病变,且狭窄程度≥50%。根据复查结果将研究对象分为ISR组(45例)和非ISR组(198例)。

1.4 观察指标 (1)TyG指数^[6]:TyG指数=Ln[空腹甘油三酯(triglyceride,TG)(mg/dl)×空腹血糖(fasting blood glucose,FBG)(mg/dl)/2]。(2)多支血管病变^[7]:三支主要冠状动脉(左前降支、左回旋支、右冠脉)及其第一级分支(如对角支、钝缘支、后降支、后侧支等分支,血管直径≥2 mm)中有2支及以上血管狭窄率≥70%。(3)Gensini评分^[8]:采用Gensini评分评估患者冠状动脉病变严重程度,每一血管节段相对应的狭窄程度积分乘以该血管相对应权重系数,即为该处病变程度的评分,各病变血管积分相加所得值即为该患者Gensini评分。(4)弥漫性病变:冠脉血管(直径≥2 mm)狭窄程度>50%,狭窄病变长度>20 mm。(5)生化指标:包括术前的总胆固醇(total cholesterol,TC)、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)]、尿酸(uric acid,UA)、肾小球滤过率(estimated glomerular filtration rate,eGFR)、FBG等血清学指标和患者术后复查冠状动脉造影时的TG、FBG水平。均经罗氏Cobas6000全自动分析仪器检测获得。(6)手术相关指标:植入支架总数、植入支架规格(直径和长度)、病变血管支数等。

1.5 统计学方法 应用 SPSS25.0 统计软件进行数据分析。符合正态分布的计量资料以均数±标准差($\bar{x} \pm s$)表示,两组间比较采用成组t检验;不符合正态分布的计量资料以中位数(下四分位数,上四分位数)[$M(P_{25}, P_{75})$]表示,两组间比较采用Mann-Whitney U检验。计数资料以例数(百分率)[n(%)]表示,组间比较采用 χ^2 检验。采用二元 logistic 回归分析探讨影响患者PCI术后发生ISR的危险因素。 $P < 0.05$ 为差异有统计学意义。

表1 两组临床资料比较[$(\bar{x} \pm s)$, $M(P_{25}, P_{75})$, n(%)]

组别	例数	性别		年龄 (岁)	吸烟	合并糖尿病	合并高血压	BMI (kg/m ²)	Gensini 评分 (分)
		男	女						
ISR组	45	36	9	62.76 ± 11.84	33(73.33)	29(64.44)	25(55.56)	23.96 ± 2.62	65.13 ± 34.70
非 ISR组	198	143	55	60.50 ± 10.95	66(33.33)	55(27.78)	128(64.65)	24.12 ± 3.11	69.04 ± 34.94
$t/\chi^2/Z$	-	1.143		1.229	24.300	21.795	1.299	0.327	0.678
P	-	0.285		0.220	0.000	0.000	0.254	0.744	0.498
组别	例数	植入支架数≥2枚		植入支架直径(mm)		植入支架长度(mm)		多支血管病变	弥漫性病变
ISR组	45	29(64.44)		3.00(2.75,3.50)		30.00(25.00,35.00)		30(66.67)	10(22.22)
非 ISR组	198	98(49.50)		3.25(2.75,3.50)		30.00(25.00,35.00)		137(69.19)	54(27.27)
$t/\chi^2/Z$	-	5.424		0.950		0.770		0.109	0.482
P	-	0.070		0.342		0.441		0.742	0.487

2.2 两组 PCI 术前和复查造影时生化指标比较 在术前,ISR组的TC、TG、FBG 和 TyG 指数水平高于非 ISR组,差异均有统计学意义($P < 0.05$)。在复查造影时,ISR组 TyG 指数水平和 TyG 指数未达标人数比例大于非 ISR组,差异均有统计学意义($P < 0.05$)。见表2。

表2 两组 PCI 术前和复查造影时生化指标比较[$(\bar{x} \pm s)$, $M(P_{25}, P_{75})$, n(%)]

组别	例数	术前							复查造影时		
		TC (mmol/L)	TG (mmol/L)	HDL-C (mmol/L)	LDL-C (mmol/L)	LP(a) (mg/dL)	UA (μmol/L)	eGFR [ml/(min·1.73 m ²)]	FBG (mmol/L)	TyG 指数	
ISR组	45	5.02 ± 1.20	2.35(1.90,2.79)	1.08 ± 0.24	2.85 ± 0.99	11.10(7.05,25.10)	398.24 ± 101.95	84.72 ± 18.63	6.32(5.71,7.89)	9.45 ± 0.40	9.30 ± 0.31
非 ISR组	198	4.52 ± 1.25	1.47(1.11,2.22)	1.12 ± 0.33	2.88 ± 1.06	11.50(6.58,26.80)	393.51 ± 118.76	85.96 ± 17.84	5.71(4.98,7.01)	9.00 ± 0.71	8.66 ± 0.81
$t/\chi^2/Z$	-	2.447	2.467	0.769	0.186	0.379	0.248	0.416	3.092	5.783	8.724
P	-	0.015	0.014	0.443	0.853	0.704	0.805	0.678	0.002	0.000	0.000

注: * TyG 指数 ≥ 9.04 为未达标

表3 冠心病患者PCI术后发生ISR的危险因素分析结果

变量	B	SE	Wald	OR(95% CI)	P
吸烟	1.886	0.445	17.934	6.592 (2.754~15.777)	0.000
合并糖尿病	1.346	0.453	8.848	3.843 (1.583~9.330)	0.003
术前 TC	0.307	0.180	2.924	1.359 (0.956~1.933)	0.087
术前 TyG 指数	-0.256	0.386	0.439	0.774 (0.364~1.649)	0.507
复查 TyG 指数	-0.651	0.451	2.086	0.522 (0.216~1.262)	0.149
复查时 TyG 指数未达标	3.147	0.717	19.269	23.273 (5.709~94.872)	0.000

2 结果

2.1 两组临床资料比较 ISR组吸烟、合并糖尿病人数比例高于非 ISR组,差异有统计学意义($P < 0.05$)。两组在年龄、性别、合并高血压病、体质量指数(body mass index,BMI)、Gensini 评分、支架植入总数、植入支架直径、植入支架长度、多支血管病变和弥漫性病变等方面比较差异均无统计学意义($P > 0.05$)。见表1。

2.3 冠心病患者PCI术后发生ISR的危险因素分析结果 以患者PCI术后发生ISR情况作为因变量(ISR = 1,非 ISR = 0),纳入表1、表2中有统计学意义的指标作为自变量,二元多因素 logistic 回归分析结果显示,吸烟、合并糖尿病、复查时 TyG 指数未达标是冠心病患者PCI术后发生ISR的独立危险因素。见表3。

3 讨论

3.1 PCI 作为目前冠心病的主要治疗手段之一,已广泛应用于临床。虽然支架工艺、手术技术、术后药物治疗等方面在近年取得了进步,但是 ISR 仍是影响 PCI 治疗效果的重要因素。药物洗脱支架的引进很大程度上解决了金属裸支架的局限性,但 ISR 发生率仍有 5%~10%^[9]。本研究纳入研究对象的 PCI 术后 ISR 发生率为 18.52%,高于相关文献报道,考虑可能与部分状态良好的患者术后未能遵医嘱随访有关。

3.2 胰岛素与其受体结合可激活下游细胞内信号通路,从而调节营养代谢、体液稳态、生长发育、离子转运、维持血管舒张等^[10-11]。长期胰岛素抵抗状态可导致高血糖、高胰岛素血症和以循环 TG 升高、HDL-C 降低为特征的脂质代谢紊乱^[12]。以平滑肌细胞从基质向内膜增殖和迁移为特征的内膜增生是 ISR 发生的主要机制^[13]。而胰岛素抵抗者机体的高血糖水平促进了晚期糖基化终末产物的形成,通过同源受体信号转导促进平滑肌细胞增殖^[14]。另外,胰岛素还可通过丝裂原活化蛋白激酶信号通路促进新生内膜增生^[15],从而导致 ISR 发生。高胰岛素-正葡萄糖钳夹试验和胰岛素抵抗的稳态模式评估法,因操作困难、价格昂贵、耗时等缺点,不适合在临幊上推广^[16]。TG 和 FBG 是临幊常规检测项目,由其二者计算得到的 TyG 指数获取容易。有研究表明,TyG 指数与用高胰岛素-正葡萄糖钳夹试验评估获得的胰岛素抵抗结果具有显著相关性,甚至评估效能更优^[6,17]。鉴此,TyG 指数被提出作为胰岛素抵抗的替代指标^[18-19]。其除了能更好地评估胰岛素抵抗外,还与其他代谢异常或疾病也具有关联,包括心脏代谢、冠心病、冠状动脉病变和心血管疾病不良预后等^[16,20-22]。Zhu 等^[20]研究发现,对于接受 PCI 治疗的急性心肌梗死患者,TyG 指数升高是术后发生 ISR 的危险因素。本研究结果显示,无论是在术前还是术后,ISR 组的 TyG 指数水平均显著高于非 ISR 组,且在术后复查时 ISR 组 TyG 指数不达标的人数比例显著高于非 ISR 组。多因素 logistic 回归分析结果也显示,患者 PCI 术后 TyG 指数未达标是发生 ISR 的独立危险因素。

3.3 本研究结果显示,吸烟、合并糖尿病是 PCI 术后 ISR 发生的独立危险因素,与既往研究相符^[23-24]。吸烟可损伤血管内皮,使血流速度减慢,促进动脉粥样硬化和加速血栓形成,从而促进 ISR 发生^[25]。有研究显示,糖尿病患者的心血管疾病发病率是非糖尿病患者 的 2~8 倍,且合并糖尿病是心血管疾病患者死亡的主要危险因素^[26]。由于新生内膜过度增生、血液高凝状态、炎症反应激活、内皮功能障碍的出现,糖尿病患者发生 ISR 的风险更高^[27]。另外,由于机体高血糖水平可促进胰岛细胞释放过量胰岛素,而持续性的高胰岛素水平会使循环中的 TG 升高、HDL-C 浓度降低,形成恶性循环,加重糖尿病患者的脂质代谢异常和胰岛素抵抗^[28]。因此,冠心病患者 PCI 治疗后的吸烟和血糖管理至关重要。

综上所述,TyG 指数升高可增加冠心病患者 PCI 术后发生 ISR 的风险,PCI 术后应加强患者控制 TyG

指数的管理,同时吸烟和血糖管理也至关重要。但研究结论仍需进一步通过大样本量的多中心研究加以验证。

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[收稿日期 2022-04-11] [本文编辑 余军伟]

本文引用格式

陈玲玲, 李波. 甘油三酯葡萄糖指数与冠心病患者经皮冠状动脉介入术后发生支架内再狭窄的关联性研究 [J]. 中国临床新医学, 2022, 15(7):631–635.