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· 论著 ·

血脂指标动态变化与冠心病患者择期经皮冠状动脉介入术后非靶血管病变进展的关系研究

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【摘要】 背景 冠心病(CHD)患者采用经皮冠状动脉介入治疗(PCI)具有确切效果,但存在靶血管支架再狭窄和非靶血管病变进展问题。**目的** 探讨血脂指标动态变化与CHD患者择期PCI后非靶血管病变进展的关系。**方法** 选取2017年1月—2019年5月空军军医大学第一附属医院心内科择期PCI后二次入院的CHD患者150例,根据非靶血管病变进展情况分为进展组45例和无进展组105例。比较两组患者性别、年龄、民族(包括回族、汉族)、吸烟情况、既往史(高血压、糖尿病)、CHD家族史、体质指数(BMI)、随访时间及syntax积分及第1次入院、第2次入院血脂指标〔包括总胆固醇(TC)、三酰甘油(TG)、高密度脂蛋白胆固醇(HDL-C)、低密度脂蛋白胆固醇(LDL-C)、非高密度脂蛋白胆固醇(non-HDL-C)、TG/HDL-C及non-HDL-C/HDL-C〕;CHD患者择期PCI后非靶血管病变进展的影响因素分析采用多因素Logistic回归分析;绘制受试者工作特征(ROC)曲线以评价non-HDL-C对CHD患者择期PCI后非靶血管病变进展的预测价值。**结果** 进展组患者女性比例、糖尿病发生率、syntax积分高于无进展组,第1次入院TC、TG、non-HDL-C低于无进展组,两次入院TC、TG、LDL-C、non-HDL-C、TG/HDL-C、non-HDL-C/HDL-C差值高于无进展组($P<0.05$)。多因素Logistic回归分析结果显示,性别〔 $OR=0.302$, 95% $CI(0.122, 0.751)$ 〕、糖尿病〔 $OR=2.946$, 95% $CI(1.222, 7.102)$ 〕、non-HDL-C动态变化〔 $OR=1.900$, 95% $CI(1.131, 3.192)$ 〕、TG/HDL-C动态变化〔 $OR=1.506$, 95% $CI(1.024, 2.215)$ 〕是CHD患者择期PCI后非靶血管病变进展的独立影响因素($P<0.05$)。ROC曲线分析结果显示,non-HDL-C动态变化与TG/HDL-C动态变化预测CHD患者择期PCI后非靶血管病变进展的曲线下面积(AUC)比较,差异无统计学意义($P>0.05$)。**结论** non-HDL-C动态变化、TG/HDL-C动态变化是CHD患者择期PCI后非靶血管病变进展的独立影响因素,且其对CHD患者择期PCI后非靶血管病变进展有一定的预测价值。

【关键词】 冠心病;冠状动脉非靶血管病变;经皮冠状动脉介入治疗;血脂指标;非高密度脂蛋白胆固醇;总胆固醇;高密度脂蛋白胆固醇

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Relationship between Dynamic Changes of Blood Lipid Indexes and Progression of Non-target Vascular Lesions in Patients with Coronary Heart Disease after Elective Percutaneous Coronary Intervention YANG Quanming, GUO Wenyi

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【Abstract】 Background Although percutaneous coronary intervention (PCI) has a significant effect in the treatment of coronary heart disease (CHD), there are still problems with stent restenosis in target vessels and progression of non-target vessel lesions. **Objective** To discuss the relationship between dynamic changes of blood lipid indexes and progression of non-target vascular lesions in patients with CHD after elective PCI. **Methods** From January 2017 to May 2019, 150 patients with CHD who were admitted for the second time after elective PCI in the Department of Cardiology, the First Affiliated Hospital of Air Force Military Medical University were selected, and they were divided into progression group ($n=45$) and non-progression group ($n=105$) according to the progression of non-target vascular lesions. Gender, age, nationality (including Hui and Han nationality), smoking, past history (including hypertension, diabetes), family history of CHD, body mass index (BMI), follow-up time and syntax score, blood lipid indexes of the 1st and 2nd admission [including total cholesterol

(TC), triacylglycerol (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), non-HDL-C, TG/HDL-C and non-HDL-C/HDL-C] were compared between the two groups. Multivariate Logistic regression analysis was used to analyse the influencing factors of non-target vascular lesions progression in patients with CHD after elective PCI. ROC curve was drawn to evaluate the predictive value of non-HDL-C on the progression of non-target vascular lesions in patients with CHD after elective PCI. **Results** Female ratio, incidence of diabetes and syntax score in progression group were higher than those in non-progression group, TC, TG, non-HDL-C of 1st admission in progression group were lower than those in non-progression group, the differences of TC, TG, LDL-C, non-HDL-C, TG/HDL-C, non-HDL-C/HDL-C between two admissions in progression group were higher than those in non-progressive group ($P < 0.05$). Multivariate Logistic regression analysis showed that, gender [$OR = 0.302$, 95%CI (0.122, 0.751)], diabetes [$OR = 2.946$, 95%CI (1.222, 7.102)], dynamic changes of non-HDL-C [$OR = 1.900$, 95%CI (1.131, 3.192)] and dynamic changes of TG/HDL-C [$OR = 1.506$, 95%CI (1.024, 2.215)] were independent influencing factors of non-target vascular lesions in patients with CHD after elective PCI ($P < 0.05$). ROC curve analysis showed that, there was no significant difference in the AUC between the dynamic changes of non-HDL-C and TG/HDL-C in predicting the progression of non-target vascular lesions progression in patients with CHD after elective PCI ($P > 0.05$). **Conclusion** The dynamic changes of non-HDL-C and TG/HDL-C are independent risk factors of non-target vascular lesions progression in patients with CHD after elective PCI, and they have a certain value in predicting the progression of non-target vascular lesions.

【Key words】 Coronary heart disease; Non-target lesions of coronary artery; Percutaneous coronary intervention; Blood lipid indexes; Non-high density lipoprotein cholesterol; Total cholesterol; High density lipoprotein cholesterol

冠状动脉粥样硬化患者病情改善程度与临床获益有关, 而疾病进展与患者预后有关^[1]。因此, 检查冠状动脉粥样硬化进展情况是临床评估心血管的有效手段, 其也是预测冠心病(CHD)患者预后的重要标志物^[2-3]。血脂异常是导致动脉粥样硬化和心血管疾病进展的主要危险因素, 且动脉粥样硬化与高三酰甘油血症、低密度脂蛋白胆固醇(LDL-C)水平、高脂血症等有关^[4-5]。近年非高密度脂蛋白胆固醇(non-HDL-C)成为预测主要不良心血管事件的新标志物^[6], 且与动脉粥样硬化斑块进展密切相关^[7-8]。目前关于择期经皮冠状动脉介入治疗(PCI)后患者非靶血管病变进展影响因素的研究较少。本研究旨在探讨血脂指标动态变化与CHD患者择期PCI后非靶血管病变进展的关系, 现报道如下。

1 资料与方法

1.1 纳入与排除标准 纳入标准: (1) 采用冠状动脉造影检查(CAG)确定至少1支冠状动脉主支或主要分支狭窄 $>70\%$ (直径法)并行择期PCI, 至少间隔3个月后二次入院行CAG; (2) 植入支架为药物洗脱支架(DES); (3) PCI后规律服用CHD二级预防药物; (4) 两次入院资料完整。排除标准: (1) 既往行冠状动脉搭桥术者; (2) 合并其他心脏疾病者; (3) 首次出院3个月内再次行PCI者; (4) 首次因急性心肌梗死而入院行PCI者; (5) 合并肝肾功能不全、恶性肿瘤、免疫系统疾病者; (6) 合并其他影响冠状动脉血管评估及血脂代谢等疾病者。

1.2 相关定义 首次行择期PCI并给予支架植入治疗的病变冠状动脉血管为靶血管, 靶血管以外的冠状动脉血管为非靶血管。CHD患者血管情况采用syntax score在线软件(<http://www.syntaxscore.com>)进行评估, 根

据CAG结果将首次入院患者的非靶血管病变评分计为syntax积分1, 间隔3个月后入院患者的非靶血管病变评分计为syntax积分2, 以syntax积分2-syntax积分1 >0 分为非靶血管病变进展, ≤ 0 分为非靶血管病变无进展。

1.3 一般资料 选取2017年1月—2019年5月空军军医大学第一附属医院心内科择期PCI后二次入院的CHD患者150例, 根据非靶血管病变进展情况分为进展组45例和无进展组105例。

1.4 观察指标

1.4.1 临床资料 收集入组患者性别、年龄、民族(包括回族、汉族)、吸烟情况、既往史(高血压、糖尿病)、CHD家族史、体质指数(BMI)、随访时间及syntax积分。

1.4.2 血脂指标 分别于患者第1次入院行PCI前、第2次入院行CAG检查前采集清晨空腹(禁食8h及以上)静脉血4ml, 应用迈瑞全自动生化分析仪检测总胆固醇(TC)、三酰甘油(TG)、高密度脂蛋白胆固醇(HDL-C)、LDL-C, 并根据检测结果计算non-HDL-C、TG/HDL-C及non-HDL-C/HDL-C, 其中non-HDL-C=TC-HDL-C。

1.5 统计学方法 采用SPSS 25.0统计学软件进行数据处理。符合正态分布的计量资料以($\bar{x} \pm s$)表示, 组间比较采用两独立样本 t 检验; 计数资料以相对数表示, 组间比较采用 χ^2 检验; CHD患者择期PCI后非靶血管病变进展的影响因素分析采用多因素Logistic回归分析; 绘制受试者工作特征(ROC)曲线以评价non-HDL-C对CHD患者择期PCI后非靶血管病变进展的预测价值, ROC曲线下面积(AUC)比较采用 Z 检验。以 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 两组患者临床资料比较 两组患者年龄、民族、吸烟率、高血压发生率、有 CHD 家族史者占比、BMI 及随访时间比较, 差异无统计学意义 ($P>0.05$); 进展组患者女性比例、糖尿病发生率、syntax 积分高于无进展组, 差异有统计学意义 ($P<0.05$, 见表 1)。

2.2 两组患者血脂指标变化情况 两组患者第 1 次入院 HDL-C、LDL-C、TG/HDL-C、non-HDL-C/HDL-C, 第 2 次入院 TC、TG、HDL-C、LDL-C、non-HDL-C、TG/HDL-C、non-HDL-C/HDL-C 及两次入院 HDL-C 差值比较, 差异无统计学意义 ($P>0.05$); 进展组患者第 1 次入院 TC、TG、non-HDL-C 低于无进展组, 入院 TC、TG、LDL-C、non-HDL-C、TG/HDL-C、non-HDL-C/HDL-C 差值大于无进展组, 差异有统计学意义 ($P<0.05$, 见表 2)。

2.3 多因素 Logistic 回归分析 将性别 (赋值: 女 =0, 男 =1)、糖尿病 (赋值: 无 =0, 有 =1)、syntax 积分 (赋值: 实测值) 及 TC 动态变化、TG 动态变化、LDL-C 动态变化、non-HDL-C 动态变化、TG/HDL-C 动态变化、non-HDL-C/HDL-C 动态变化 (赋值: 均为实测值差值) 作为自变量, 非靶血管病变进展情况 (赋值: 未

进展 =0, 进展 =1) 为因变量行多因素 Logistic 回归分析, 结果显示, 性别、糖尿病、non-HDL-C 动态变化、TG/HDL-C 动态变化是 CHD 患者择期 PCI 后非靶血管病变进展的独立影响因素 ($P<0.05$, 见表 3)。

表 3 CHD 患者择期 PCI 后非靶血管病变进展影响因素的多因素 Logistic 回归分析

Table 3 Multivariate Logistic regression analysis on influencing factors of non-target vascular lesion progression in patients with CHD after elective PCI

变量	β	SE	Wald χ^2 值	自由度	P 值	OR (95%CI)
性别	-1.196	0.464	6.644	1	0.010	0.302 (0.122, 0.751)
糖尿病	1.080	0.449	5.789	1	0.016	2.946 (1.222, 7.102)
non-HDL-C 动态变化	0.642	0.265	5.878	1	0.015	1.900 (1.131, 3.192)
TG/HDL-C 动态变化	0.409	0.197	4.320	1	0.038	1.506 (1.024, 2.215)

2.4 ROC 曲线 用 MedCalc 统计软件绘制 ROC 曲线分析结果显示, non-HDL-C 动态变化预测 CHD 患者择期 PCI 后非靶血管病变进展的 AUC 为 0.701 [95%CI (0.603, 0.800)], TG/HDL-C 动态变化预测 CHD 患者择期 PCI 后非靶血管病变进展的 AUC 为 0.657 [95%CI (0.559, 0.755)], 二者差异无统计学意义 ($Z=0.760$, $P=0.447$, 见图 1)。

表 1 两组患者临床资料比较

Table 1 Comparison of clinical data between the two groups

组别	例数	女性 [n (%)]	年龄 ($\bar{x} \pm s$, 岁)	民族 [n (%)]		吸烟 [n (%)]	既往史 [n (%)]		CHD 家族 史 [n (%)]	BMI ($\bar{x} \pm s$, kg/m ²)	随访时间 ($\bar{x} \pm s$, 月)	syntax 积分 ($\bar{x} \pm s$, 分)
				回族	汉族		高血压	糖尿病				
无进展组	105	17 (16.2)	57.3 $\pm$ 11.0	3 (2.9)	102 (97.1)	53 (50.5)	45 (42.9)	20 (19.0)	3 (2.9)	25.3 $\pm$ 3.4	12.5 $\pm$ 4.7	6.9 $\pm$ 6.3
进展组	45	15 (33.3)	59.3 $\pm$ 12.0	3 (6.7)	42 (93.3)	19 (42.2)	18 (40.0)	18 (40.0)	1 (2.2)	25.0 $\pm$ 3.2	13.4 $\pm$ 4.7	13.4 $\pm$ 8.5
$\chi^2 (t)$ 值		5.516	-0.925 ^a		0.405	0.860	0.106	7.311	0	0.515 ^a	-1.103 ^a	-4.621 ^a
P 值		0.029	0.357		0.524	0.378	0.444	0.009	1.000	0.607	0.272	<0.001

注: CHD= 冠心病, BMI= 体质指数; ^a 为 t 值

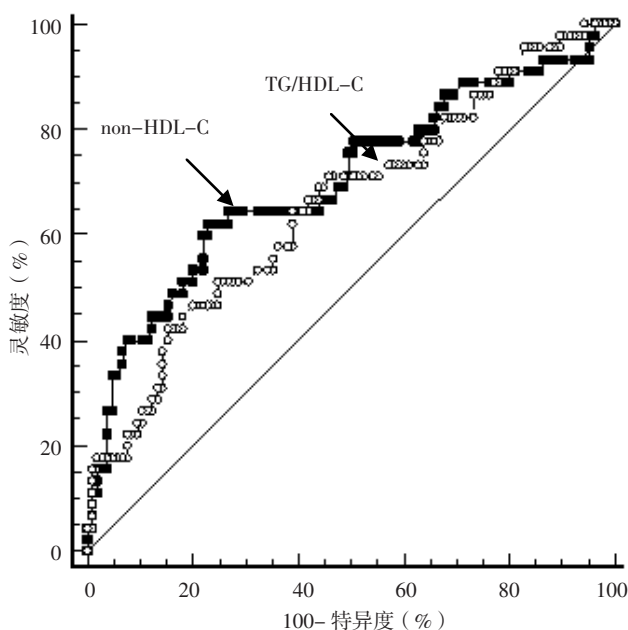
表 2 两组患者治疗前后血脂指标变化情况 ($\bar{x} \pm s$)

Table 2 Changes of blood lipid indexes between the two groups before and after treatment

组别	例数	TC (mmol/L)			TG (mmol/L)			HDL-C (mmol/L)			LDL-C (mmol/L)		
		第 1 次入院	第 2 次入院	差值	第 1 次入院	第 2 次入院	差值	第 1 次入院	第 2 次入院	差值	第 1 次入院	第 2 次入院	差值
无进展组	105	3.74 $\pm$ 1.04	3.18 $\pm$ 0.76	-0.56 $\pm$ 0.91	1.8 $\pm$ 1.0	1.5 $\pm$ 0.9	-0.2 $\pm$ 0.8	1.00 $\pm$ 0.23	1.01 $\pm$ 0.22	0.01 $\pm$ 0.22	2.06 $\pm$ 0.84	1.60 $\pm$ 0.66	-0.46 $\pm$ 0.78
进展组	45	3.32 $\pm$ 0.84	3.37 $\pm$ 0.85	0.05 $\pm$ 1.09	1.4 $\pm$ 0.7	1.9 $\pm$ 1.5	0.5 $\pm$ 1.4	0.97 $\pm$ 0.22	1.01 $\pm$ 0.30	0.05 $\pm$ 0.19	1.85 $\pm$ 0.69	1.80 $\pm$ 0.78	-0.04 $\pm$ 0.93
t 值		2.363	-1.365	-3.517	2.102	-1.606	-3.303	0.814	-0.159	-1.059	1.512	-1.666	-2.852
P 值		0.019	0.174	0.001	0.037	0.114	0.002	0.417	0.874	0.292	0.133	0.098	0.005

组别	non-HDL-C (mmol/L)			TG/HDL-C			non-HDL-C/HDL-C		
	第 1 次入院	第 2 次入院	差值	第 1 次入院	第 2 次入院	差值	第 1 次入院	第 2 次入院	差值
无进展组	2.74 $\pm$ 1.00	2.17 $\pm$ 0.72	-0.56 $\pm$ 0.85	1.94 $\pm$ 1.60	1.63 $\pm$ 1.06	-0.31 $\pm$ 1.20	2.88 $\pm$ 1.52	2.25 $\pm$ 0.89	-0.640 $\pm$ 1.230
进展组	2.36 $\pm$ 0.78	2.39 $\pm$ 0.76	0.03 $\pm$ 0.97	1.59 $\pm$ 0.94	2.29 $\pm$ 2.46	0.70 $\pm$ 2.16	2.53 $\pm$ 0.90	2.53 $\pm$ 1.00	0.003 $\pm$ 0.960
t 值	2.276	-1.671	-3.800	1.371	-1.724	-2.939	1.448	-1.736	-3.079
P 值	0.024	0.097	<0.001	0.173	0.091	0.005	0.150	0.085	0.002

注: TC= 总胆固醇, TG= 三酰甘油, HDL-C= 高密度脂蛋白胆固醇, LDL-C= 低密度脂蛋白胆固醇, non-HDL-C= 非高密度脂蛋白胆固醇



注: non-HDL-C= 非高密度脂蛋白胆固醇, TG/HDL-C= 三酰甘油 / 高密度脂蛋白胆固醇

图1 non-HDL-C动态变化和TG/HDL-C动态变化对CHD患者择期PCI后非靶病变进展预测价值的ROC曲线

Figure 1 ROC curve of predictive value of non-HDL-C and TG/HDL-C dynamic changes on non-target lesion progression in CHD patients after elective PCI

3 讨论

动脉粥样硬化是冠状动脉非靶血管病变进展的病理基础,与高血压、年龄、异位肥胖、糖尿病、血脂异常、吸烟、久坐、内皮、血管、激素水平和凝血功能等有关^[9-12],其中血脂异常是动脉粥样硬化的主要危险因素,因此早期诊断和管理相关因素是预防动脉粥样硬化发生、发展的关键^[13]。

non-HDL-C是由TC减去HDL-C计算而得,包括LDL-C、极低密度脂蛋白胆固醇、中间密度脂蛋白胆固醇、脂蛋白a和乳糜微粒等所有致动脉粥样硬化性脂蛋白颗粒中的胆固醇,检测方便且不受饮食限制,已被公认为治疗高三酰甘油血症或心脏代谢异常患者的靶标志物。一项对接受他汀类药物治疗的患者进行的荟萃分析结果显示,降低non-HDL-C水平可降低患者主要不良心血管事件发生风险^[14]。一项大规模的参与水平分析结果显示,non-HDL-C较LDL-C更能作为评估主要不良心血管事件风险的标志物^[15]。有学者对连续接受CAG但未接受任何降脂治疗的患者进行了研究,结果表明,在冠状动脉粥样硬化患者中,non-HDL-C与冠状动脉粥样硬化的关系较LDL-C更为密切;在预测患者冠状动脉粥样硬化严重程度方面,non-HDL-C优于LDL-C^[16-17]。然而,non-HDL-C与CHD患者PCI后冠状动脉非靶血管病变进展间有怎样的关系、HDL-C及

其与致动脉粥样硬化血脂成分(包括TG、non-HDL-C)比值对非靶血管病变进展有何影响目前尚无定论。

本研究结果显示,进展组患者第1次入院TC、TG和non-HDL-C水平低于无进展组,且两次入院TC、TG、LDL-C、non-HDL-C、TG/HDL-C、non-HDL-C/HDL-C差值大于无进展组,表明血脂水平动态变化对于CHD患者择期PCI后非靶血管病变进展具有参考意义。此外,两组患者HDL-C水平在第1次入院、第2次入院及其差值间均无统计学差异,表明即使HDL-C水平在参考范围内,CHD患者非靶血管病变进展风险仍然存在。研究表明,正常水平LDL-C、HDL-C人群CHD发病率仍较高^[18-19]。本研究结果显示,性别是CHD患者择期PCI后非靶血管病变进展的独立影响因素。研究表明,女性CHD发生风险低于男性^[20];另有研究表明,雌激素在冠状动脉血管反应活性中具有保护作用,并可通过抗炎作用促进斑块稳定^[21],但目前性别与CHD间的关系尚存在争议。本研究结果显示,糖尿病是CHD患者择期PCI后非靶血管病变进展的独立影响因素。研究指出,与非糖尿病患者相比,男性成年糖尿病患者心脏病发病率较其高2.5倍,女性较其高2.4倍^[22]。2017年一项荟萃分析结果显示,与糖化血红蛋白<7.0%的糖尿病患者相比,糖化血红蛋白 $\geq 7.0\%$ 的糖尿病患者心血管疾病死亡风险较其高85%〔OR=1.85, 95%CI(1.14, 2.55)〕。另有研究表明,与糖化血红蛋白<6.0%的非糖尿病患者相比,糖化血红蛋白 $\geq 6.0\%$ 的非糖尿病患者心血管疾病死亡发生风险较其高50%〔OR=1.50, 95%CI(1.01, 2.21)〕^[23]。心血管疾病是糖尿病患者发病和死亡的主要原因^[24]。

本研究结果还显示,non-HDL-C变化、TG/HDL-C变化是CHD患者择期PCI后非靶血管病变进展的独立影响因素;ROC曲线分析显示,non-HDL-C变化、TG/HDL-C变化预测CHD患者择期PCI后非靶血管病变进展的AUC间无统计学差异,表明non-HDL-C动态变化和TG/HDL-C动态变化对CHD患者择期PCI后非靶血管病变的预测价值无明显差异。

综上所述,non-HDL-C动态变化、TG/HDL-C动态变化是CHD患者择期PCI后非靶血管病变进展的独立影响因素,且对CHD患者择期PCI后非靶血管病变进展均有一定的预测价值;但本研究为回顾性研究,且样本量较少,结果结论可能存在选择性偏倚,后续需进一步行多中心联合、大样本量、前瞻性研究验证本研究结论。

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