非糖尿病急性冠脉综合征住院患者 HDL-C、LDL-C/HDL-C 水平回顾性分析

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摘 要:【目的】回顾性分析非糖尿病急性冠脉综合征 HDL-C、LDL-C/HDL-C 水平及冠脉病变相关性。【方法】选择本院 2011.05-2015.05 住院符合急性冠脉综合征诊断标准并无 2 型糖尿病患者 306 例为研究对象，选择同期住院符合急性冠脉综合征诊断标准并确诊为 2 型糖尿病患者 174 例,以及冠脉造影正常无糖尿病患者 258 例为对照,所有患者均行冠状动脉造影检查。将前降支、回旋支或右冠脉中任何一支狭窄≥50%为单支病变组;前降支、回旋支或右冠脉中任何两支病变≥50%及左主干病变为双支病变组；将前降支、回旋支和右冠状动脉三支病变均≥50%或左主干合并右冠脉病变为多支病变组。搜集临床资料及生化血脂指标,采用 SPSS18.0 进行统计分析。【结果】①非糖尿病急性冠脉综合征组和 2 型糖尿病急性冠脉综合征组,HDL-C 水平均低于冠脉正常组,而 LDL-C/HDL-C 均高于冠脉正常组($P < 0.05$);②非糖尿病急性冠脉综合征患者中,冠脉双支病变组、多支病变组 HDL-C 水平均低于单支病变组($P < 0.05$);而多支病变组 LDL-C/ HDL-C 均显著高于单支病变组、双支病变组($P < 0.05$)。③非糖尿病急性冠脉综合征患者冠脉病变支数与 HDL-C 水平呈负相关($r = -0.199$, $P < 0.001$),与 LDL-C/HDL-C 水平呈正相关($r = 0.184$, $P = 0.001$)。【结论】低 HDL-C、高 LDL-C/HDL-C 可作为冠心病预测指标之一。非糖尿病急性冠脉综合征患者冠脉病变严重程度与 HDL-C、LDL-C/HDL-C 密切相关。

关键词:非糖尿病;急性冠脉综合征;HDL-C;LDL-C/HDL-C

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Retrospective Analysis on HDL-C and LDL-C/HDL-C Level in Non-diabetic Acute Coronary Syndrome Patients

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Abstract:【Objectives】To retrospectively analyze the correlation on HDL-C, LDL-C/HDL-C level and coronary lesions in non-diabetic acute coronary syndrome (ACS) subjects.【Methods】306 patients which hospitalized in Cardiology Department of Sun Yat-sen Memorial Hospital of Sun Yat-sen University from May 2011 to May 2015 with diagnosed acute coronary syndrome (ACS) and without type 2 diabetes mellitus were recruited as Non-diabetic ACS group, another 174 patients which hospitalized and were diagnosed with acute coronary syndrome with type 2 diabetes mellitus as diabetic ACS group and 258 subjects with normal coronary angiography and non-type 2 diabetes mellitus in the same period as control group were also recruited. All subjects were accepted

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coronary angiography examination on coronary artery. According to the coronary angiography results, only one vessel of the left anterior descending artery (LAD), left circumflex artery (LCX) or right coronary artery (RCA) stenosis was above 50% were selected as single-vessel? lesion group, and patients that confirmed two vessels of the LAD, LCX, RCA or left main coronary artery obstructive were selected as two-vessel lesion group, patients that showed three of LAD, LCX, RCA or two of left main coronary artery and right coronary artery obstructive were selected as multi-vessel lesion group. All the data were analyzed by SPSS18.0. 【Results】 (1) Compared with control group, the HDL-C level was significantly decreased, and LDL-C/HDL-C was significantly increased both in Non-diabetic ACS group and diabetic-ACS group ($P < 0.05$, respectively); (2) In non-diabetic ACS subjects, the HDL-C level was significantly decreased in two-vessel lesions group and multi-vessel lesions group than that in single-vessel lesions group ($P < 0.05$, respectively). However, the LDL-C/HDL-C were significantly increase in single-vessel lesion group and two-vessel lesion group than that in multi-vessel lesions group ($P < 0.05$); (3) In non-diabetic ACS group, the artery stenosis vessel number was inversely correlated with HDL-C level ($r = -0.199$, $P < 0.001$), but positively correlated with LDL-C/HDL-C level ($r = 0.184$, $P < 0.001$). 【Conclusions】 In non-diabetic ACS patients, both HDL-C and LDL-C/HDL-C might be the indicators of coronary disease. Low HDL-C level and high LDL-C/HDL-C might play an important role in the severity of coronary lesion.

Key words: non-diabetic disease; acute coronary syndrome (ACS); HDL-C; LDL-C/HDL-C

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急性冠脉综合征 (acute coronary syndrome, ACS)是冠心病(coronary heart disease,CHD)其中的一种类型，是指在冠状动脉粥样硬化基础上斑块不稳定、发生破裂引起冠状动脉阻塞病变为病理基础的一组临床综合征。研究证实,高密度脂蛋白胆固醇(high density lipoprotein cholesterol,HDL-C)与冠心病发病风险呈负相关,而低密度脂蛋白胆固醇(low density lipoprotein cholesterol,LDL-C)是冠心病发病的独立危险因素，与冠心病发病风险呈正相关[1-2]。LDL-C/HDL-C 是评价冠状动脉粥样硬化的重要指标之一[1,3]。有一项新靶向治疗试验主要研究服用他汀类药物 3 个月后血脂水平与心血管事件的相关性研究发现，随着 LDL-C/HDL-C 比值增加冠心病发病风险显著增加,因此考虑 LDL-C/HDL-C 可能是评估心血管事件的另一重要指标[4]。糖尿病是增加冠心病发病率和死亡率的主要原因之一[5-6],也可导致血脂代谢紊乱[7]。临床观察中发现越来越多非糖尿病急性冠脉综合征患者，而非糖尿病状态下急性冠脉综合征患者 HDL-C、LDL-C/HDL-C 水平变化如何,目前国内外的研究报道仍然较少，因此本文回顾性分析非糖尿病急性冠脉综合征 HDL-C、LDL-C/HDL-C 水平及冠脉病变相关性。

1　材料与方法

1.1　研究对象

选择 2011 年 5 月 30 日-2015 年 5 月 30 日心血管内科诊断为急性冠脉综合征(包括急性 ST 段抬高性心肌梗死、急性非 ST 抬高性心肌梗死和不稳定型心绞痛）的患者行冠状动脉造影，将前降支、回旋支或右冠脉中任何一支狭窄≥50%为单支病变组;前降支、回旋支或右冠脉中任何两支病变≥50%及左主干病变为双支病变组;将前降支、回旋支和右冠状动脉三支病变均≥50%或左主干合并右冠脉病变为多支病变组。将符合急性冠脉综合征诊断标准并无 2 型糖尿病患者 306 例为研究对象，选择同期住院符合急性冠脉综合征诊断标准并确诊为 2 型糖尿病患者 174 例，以及冠脉造影正常无糖尿病患者 258 例为对照。排除严重慢性肝功能不全、甲状腺功能亢进、甲状腺功能减退、肿瘤、结缔组织病、风心病、心肌病、肺心病及既往有记录调脂药物应用史。

1.2　研究方法

登记所有符合入选条件患者的性别、年龄、发病至入院时间、主诉、吸烟饮酒史、身高、体质量、血压、既往病史等一般资料。空腹 12 h,次日清晨 08:00 空腹采血,送检我院检验科,完成肝、肾功能、总胆固醇(total cholesterol, TC)、甘油三酯(triglyceride, TG)、HDL-C、LDL-C、载脂蛋白 A1 (apolipoprotein A1,apoA1)、载脂蛋白 B (apolipoprotein B, apoB)、血糖、高敏 C-反应蛋白 (high sensitivity C reactive protein, hsCRP)等指标。

1.3　统计学处理

计量资料符合正态性检验,以均数±标准差表示($\bar{x} \pm s$),三组间比较用单因素方差分析(one-way

ANOVA),组间两两比较用 LSD–t 法, $P < 0.05$ 差异有统计学意义;若不满足正态性检验,以中位数(M)、四分位间距(Q_1,Q_3)表示,采用 Wilcoxon 秩和检验;计数资料用百分位数表示(%),三组间采用卡方检验分析,组间两两比较均采用 Bonferroni 法, $P < 0.05$ 差异有统计学意义。冠脉病变支数与 HDL–C、LDL–C/HDL–C 水平间采用 Spearman 相关分析。所有统计采用 SPSS 18.0 统计软件进行统计分析。

2 结 果

2.1 三组之间临床资料比较

三组之间,男性百分比、年龄、BMI、吸烟史有显著差异($P < 0.05$),而高血压史无显著差异($P > 0.05$);组间两两比较,男性百分比、吸烟史非糖尿病急性冠脉综合征组显著高于 2 型糖尿病组和冠脉正常组($P < 0.05$);而发病年龄、BMI 非糖尿病急性冠脉综合征组和 2 型糖尿病组显著高于冠脉正常组($P < 0.05$,表 1)。

2.2 三组之间 HDL–C、LDL–C/HDL–C 及血脂水平分析

采用单因素方差分析, 三组间 HDL–C、LDL–C、apoA1、apoB、TC/HDL–C、LDL–C/HDL–C、apoA1/apoB、hsCRP 水平均有统计学差异 ($P < 0.001$), TG/HDL–C 水平差异亦有统计学意义 ($P = 0.033$)。采用 LSD–t 法行两两比较,结果表明,与冠脉正常组相比,非糖尿病急性冠脉综合征组和 2 型糖尿病急性冠脉综合征组 HDL–C、apoA1/apoB 水平均低于冠脉正常组,而 LDL–C/HDL–C、hsCRP 水平均高于冠脉正常组, 差异均有统计学意义(P 均 < 0.05);非糖尿病急性冠脉综合征组 LDL–C 水平高于冠脉正常组和 2 型糖尿病急性冠脉综合征组,差异均有统计学意义(P 均 < 0.05,表2)。

表 1 三组临床资料分析

Table 1 Clinical data in three groups [n(%) or $\bar{x} \pm s$]

	Non–diabetic ACS group (n = 306)	Diabetic ACS group (n = 174)	Control group (n = 258)	F/χ^2	P
Male	70.59	51.72[1)]	52.71[1)]	27.32	< 0.001
Age/years	63.0 ± 11.2[3)]	60.6 ± 10.1[3)]	55.5 ± 10.5	11.28	< 0.001
BMI/(kg/m^2)	24.4 ± 2.8[3)]	25.1 ± 3.4[3)]	22.8 ± 3.5	7.44	0.002
Smoking	51.31	29.31[1)]	32.95[1)]	30.59	< 0.001
Hypertension	52.94	55.74	48.45	1.96	0.337

Compared to non–diabetic ACS group,1) $P < 0.05$, compare to diabetic ACS group, 2) $P < 0.05$, compare to control group, 3) $P < 0.05$

表 2 三组 HDL–C、LDL–C/HDL–C 及血脂水平分析

Table 2 HDL–C, LDL–C/HDL–C and blood lipid levels of three groups ($\bar{x} \pm s$)

	Non–diabetic ACS group (n = 306)	Diabetic ACS group (n = 174)	Control group (n = 258)	F	P
TC/(mmol/L)	5.27 ± 1.32	5.11 ± 1.12	5.03 ± 1.35	2.35	0.097
TG/(mmol/L)	2.07 ± 2.45	2.66 ± 2.05	2.00 ± 2.17	2.50	0.083
HDL–C/(mmol/L)	1.12 ± 0.29[3)]	1.08 ± 0.27[3)]	1.24 ± 0.29	16.56	<0.001
LDL–C/(mmol/L)	3.42 ± 0.98	3.11 ± 0.97[1)]	3.07 ± 0.85[1)]	0.85	<0.001
apoA1/(mmol/L)	1.09 ± 0.23	1.10 ± 0.21	1.16 ± 0.21[1)]	8.12	<0.001
apoB/ (mmol/L)	0.91 ± 0.26	0.89 ± 0.27	0.82 ± 0.23[1)]	8.45	<0.001
TC/HDL–C	4.93 ± 1.71	5.03 ± 1.68	4.24 ± 1.55[2)]	14.71	<0.001
TG/HDL–C	2.10 ± 3.32	2.63 ± 2.57	1.83 ± 2.37[2)]	3.44	0.033
LDL–C/HDL–C	3.20 ± 1.11[3)]	3.04 ± 1.17[3)]	2.57 ± 0.84	26.72	<0.001
apoA1/apoB	1.27 ± 0.39[3)]	1.32 ± 0.40[3)]	1.51 ± 0.47	22.39	<0.001
hsCRP/(mg/L)	20.7 ± 43.5[3)]	20.6 ± 44.4[3)]	3.4 ± 7.3	19.80	<0.001

Compared to non–diabetic ACS group,1)$P < 0.05$; compare to diabetic ACS group, 2) $P < 0.05$; compare to control group, 3) $P < 0.05$

2.3　非糖尿病急性冠脉综合征患者冠脉病变支数与 HDL-C、LDL-C/HDL-C 水平分析

共纳入单支病变组 123 例、双支病变组 102 例、多支病变组 81 例。采用单因素方差分析,三组间 HDL-C、apoA1、LDL-C/HDL-C 、TC/HDL-C、apoA1/apoB 水平均显著差异。采用 LSD-t 法进行两两比较,结果表明,HDL-C、apoA1 水平,双支病变组、多支病变组均低于单支病变组,差异均有统计学意义（P 均 < 0.05);LDL-C/HDL-C 水平,单支病变组、双支病变组均显著低于多支病变组,差异有统计学意义（P < 0.05);apoA1/apoB 水平,单支病变组显著高于多支病变组，而 TC/HDL-C 水平单支病变组显著低于多支病变组，差异均有统计学意义(P < 0.05,表 3)。

表 3　非糖尿病急性冠脉综合征患者不同冠脉病变 HDL-C、LDL-C/HDL-C 水平分析

Table 3　HDL-C, LDL-C/HDL-C levels by different coronary lesions in non-diabetic acute coronary syndrome

($\bar{x} \pm s$)

	Single-vessel lesions group (n = 123)	Two-vessel lesions group (n = 102)	Multi-vessel lesions group (n = 81)	F	P
TC/(mmol/L)	5.26 ± 1.08	5.21 ± 1.66	5.40 ± 1.18	0.45	0.638
TG/(mmol/L)	1.96 ± 1.16	2.25 ± 3.93	2.06 ± 1.12	0.38	0.684
HDL-C/(mmol/L)	1.19 ± 0.30	1.09 ± 0.28[1)]	1.05 ± 0.26[1)]	7.33	0.001
LDL-C/(mmol/L)	3.35 ± 0.91	3.36 ± 1.05	3.62 ± 1.01	2.06	0.129
apoA1/(mmol/L)	1.15 ± 0.24	1.06 ± 0.23[1)]	1.03 ± 0.17[1)]	8.00	<0.001
apoB /(mmol/L)	0.92 ± 0.27	0.89 ± 0.28	0.92 ± 0.21	0.37	0.691
TC/HDL-C	4.59 ± 1.16	5.03 ± 2.22	5.40 ± 1.62[1)]	5.34	0.005
TG/HDL-C	1.83 ± 1.33	2.41 ± 5.39	2.18 ± 1.63	0.85	0.429
LDL-C/HDL-C	2.93 ± 0.93[3)]	3.22 ± 1.13[3)]	3.62 ± 1.25	9.28	<0.001
apoA1/apoB	1.34 ± 0.44	1.26 ± 0.38	1.18 ± 0.32[1)]	3.98	0.020
hsCRP/(mg/L)	18.4 ± 47.7	25.1 ± 42.7	19.3 ± 39.1	0.71	0.492

Compared to Single-vessel lesions group, 1) P < 0.05; compare to Two-vessel lesions group, 2) P < 0.05; compare to multi-vessel lesions group, 3) P < 0.05

2.4　非糖尿病急性冠脉综合征患者冠脉病变支数与 HDL-C、LDL-C/HDL-C 水平分析

非糖尿病急性冠脉综合征患者，经 Spearman 等级相关分析结果表明，冠脉病变支数与 HDL-C 水平呈负相关(r = -0.199,P < 0.001),而与 LDL-C/HDL-C 水平呈正相关(r = 0.184,P = 0.001)。

3　讨　论

LDL-C/HDL-C 是评价冠状动脉粥样硬化的重要指标之一[1,3]。有一项关于冠心病患者血脂浓度与颈动脉粥样硬化斑块相关性研究表明,LDL-C/HDL-C 比单纯 HDL-C 或 LDL-C 的相关系数要高[8]。Mamabolo 等[9]一项关于血脂与体质测量指标相关性研究发现，南非黑人青少年组 BMI 19.82(4.49)和 LDL-C/HDL-C 1.75(0.79)显著低于白人组 21.39(4.85)和 2.22(0.89),差异有统计学意义(P<0.0001);而两组间 HDL-C 水平无显著差异(P=0.273);纠正性别后,黑人青少年组 BMI 与 HDL-C 呈负相关（r = -0.382,P = 0.010),与 LDL-C/HDL-C 无显著相关性（r = 0.126,P = 0.157)；白人青少年 BMI 与 LDL-C/HDL-C 呈正相关(r = 0.601,P < 0.0001),与 HDL-C 无显著相关（r = -0.149,P = 0.393)。本研究中,BMI、LDL-C/HDL-C 非糖尿病急性冠脉综合征组和 2 型糖尿病组显著高于冠脉正常组(P < 0.05);而 HDL-C 水平非糖尿病急性冠脉综合征组 1.12 ± 0.29 和 2 型糖尿病急性冠脉综合征组 1.08 ± 0.27 显著低于冠脉正常组 1.24 ± 0.29(P < 0.05)。

最近一项 Meta 分析对 REVERSAL、CAMELOT、ACTIVATE 和 ASTEROID 等 4 项临床研究分析得出如下结论：LDL-C/HDL-C>2.0 与冠脉斑块体积进展相关,而 LDL-C/HDL-C≤2 与药物干预导致斑块衰退体积变小相关[1,10]。PROSPER 研究对 6 000 个患者进行回顾性分析，发现老年人 LDL-C/HDL-C 是衡量心血管疾病风

险最强的指标，研究者还得出 LDL-C/HDL-C 的变化可作为他汀类药物治疗有效性的观察指标，并建议应针对 LDL-C/HDL-C >3.3 的人群进行他汀类药物治疗[11]。Kimura 等[1]采用血管内超声检测慢性冠心病 68 例和急性冠脉综合征 24 例冠脉斑块，研究发现慢性冠心病组中 LDL-C/HDL-C 与 LPA/non-LPA(LPA：脂质池区)呈正相关(r = 0.38，P = 0.022)，而与急性冠脉综合征组无显著相关性（r = 0.27，P = 0.21)；同时，慢性冠心病组 LDL-C/HDL-C 1.93 ± 0.73 显著低于急性冠脉综合征组 2.30 ± 0.62（P = 0.02)，而两组间 HDL-C 水平无显著差异（P = 0.67)；因此认为 LDL-C/HDL-C 可能是有效预测冠状动脉粥样硬化脂质斑块和斑块易损性的指标。本研究中，冠脉病变支数与 HDL-C 水平呈负相关（r = -0.199，P < 0.001)，而与 LDL-C/HDL-C 水平呈正相关（r = 0.184，P = 0.001)，这与 Kimura 等研究结果相近，因此考虑 LDL-C/HDL-C 与冠脉病变相关。

心脏健康饮食被认为冠心病一级预防和二级预防的重要因素[12]。2013 AHA/ACC 指南指出生活管理方式可以减少心血管疾病的风险，建议健康饮食模式应该是 5% ~ 6%热量从饱和脂肪酸中获取，从而降低 LDL-C，最终达到降低冠心病发病风险[13]。Kriengsinyos 等[14]研究证实，坚持食用添加植物甾烷醇的饼干 4 周以上可显著降低 TC、LDL-C 和 LDL-C/HDL-C 分别为 4.9%、6.1%和 4.3%(均 P < 0.05)。体育锻炼是降低冠心病发病风险的另一重要因素[11]。大量研究证实，坚持体育锻炼可有效增加 HDL-C 水平[15]。最近一项 Meta 分析也证实，持续的运动可增加 HDL-C 水平 5%-8%[2, 16]。Pattyn 等研究证实，HDL-C 水平轻微增加可减少冠心病发病风险 16%-24%[16]。Mielgo-Ayuso 等[2]研究中，22 名女性排球运动员经过 11 周运动和健康饮食，LDL-C/HDL-C 较前显著降低，而 HDL-C 水平较运动前增加，但是差异无统计学意义(P = 0.089)。此外，每周的锻炼数量与 HDL-C 水平升高和 LDL-C/ HDL-C 指数降低相关，而且发现促进脂质代谢的有效运动时间为最后 48 h[17]。

综合上述，本研究中低水平 HDL-C 和高 LDL-C/HDL-C 能更好地反映非糖尿病急性冠脉综合征患者冠脉病变严重程度；通过健康饮食和运动可以降 LDL-C 水平、LDL-C/HDL-C 及提高 HDL-C 水平，从而有效降低非糖尿病急性冠脉综合征发病率。由于本研究纳入的病例数比较少，故尚待更大、更全面的研究进一步证实。

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