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临床研究·论著

HDL-C/ApoA1、MCP-1水平与中青年冠心病患者病变程度及炎症反应的相关性*

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摘要: 目的 探讨高密度脂蛋白胆固醇(HDL-C)/载脂蛋白A1(ApoA1)及单核细胞趋化蛋白-1(MCP-1)水平与中青年冠状动脉粥样硬化性心脏病(以下简称冠心病)病变程度及炎症反应的相关性。**方法** 选取2021年10月—2022年10月在南通大学附属医院和如皋市人民医院就诊的中青年冠心病患者130例作为观察组, 其中稳定型心绞痛(SAP)42例, 不稳定型心绞痛(UAP)50例, 急性心肌梗死(AMI)38例; 病变支数: 单支病变59例, 双支病变39例, 三支病变32例; 按照狭窄程度分为轻度46例, 中度54例, 重度30例。另取同期该院冠状动脉CT血管造影或冠状动脉造影正常者130例作为对照组。比较各组HDL-C/ApoA1、MCP-1、肌酸激酶同工酶MB(CK-MB)、肌酸激酶(CK)、心肌肌钙蛋白I(cTn I)、白细胞计数(WBC)、超敏C反应蛋白(hs-CRP)、生长刺激表达基因2蛋白(ST2)及Gensini评分。**结果** 观察组HDL-C/ApoA1低于对照组($P < 0.05$), MCP-1、CK-MB、CK、cTn I、WBC、hs-CRP、ST2高于对照组($P < 0.05$)。AMI和UAP患者的HDL-C/ApoA1低于SAP患者($P < 0.05$), MCP-1、CK-MB、CK、cTn I高于SAP患者($P < 0.05$)。SAP、UAP、AMI患者的WBC、hs-CRP、ST2比较, 差异均无统计学意义($P > 0.05$)。双支和三支病变患者的HDL-C/ApoA1低于单支病变患者($P < 0.05$), MCP-1、CK-MB、CK、cTn I高于单支病变患者($P < 0.05$)。不同病变支数患者的WBC、hs-CRP、ST2比较, 差异均无统计学意义($P > 0.05$)。中、重度患者的HDL-C/ApoA1低于轻度患者($P < 0.05$), MCP-1、CK-MB、CK、cTn I、WBC、hs-CRP、ST2高于轻度患者($P < 0.05$)。观察组HDL-C/ApoA1与CK-MB、CK、cTn I、WBC、hs-CRP、ST2及Gensini评分均呈负相关($P < 0.05$); MCP-1与CK-MB、CK、cTn I、WBC、hs-CRP、ST2及Gensini评分均呈正相关($P < 0.05$)。**结论** 中青年冠心病患者HDL-C/ApoA1降低, MCP-1升高。HDL-C/ApoA1、MCP-1水平与疾病类型、病变支数及病情严重程度有关, 其水平与患者炎症反应有相关性。

关键词: 冠状动脉粥样硬化性心脏病; 高密度脂蛋白胆固醇; 载脂蛋白A1; 单核细胞趋化蛋白-1; 中青年; 病变程度; 炎症反应

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Correlation of the HDL-C/ApoA1 ratio and the level of MCP-1 with severity of coronary heart disease and inflammatory response in young and middle-aged people*

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Abstract: Objective To investigate the correlation of the high-density lipoprotein cholesterol (HDL-C)/apolipoprotein A1 (ApoA1) ratio and the level of monocyte chemoattractant protein-1 (MCP-1) with the severity of coronary heart disease and inflammatory response in young and middle-aged people. **Methods** A total of 130 young and middle-aged patients with coronary heart disease treated in Affiliated Hospital of Nantong University and Rugao People's Hospital from October 2021 to October 2022 were selected as the observation group, including 42 patients with stable angina pectoris (SAP), 50 patients with unstable angina pectoris (UAP) and 38 patients with acute myocardial infarction (AMI). Regarding the number of branches of the coronary artery involved, 59 cases had one branch involvement, 39 cases two branches involvement, and 32 cases three branches involvement. Besides, 46, 54 and 30 patients showed mild, moderate and severe stenosis of the coronary artery. At the same time, 130 patients with normal findings on coronary computed tomography angiography (CTA) or coronary angiography in the hospitals were selected as the control group. The HDL-C/ApoA1 ratio, and the levels of MCP-1, creatine kinase MB (CK-MB), creatine kinase (CK), cardiac troponin I (cTnI), high-sensitivity C-reactive protein (hs-CRP), and growth stimulating expressed gene 2 (ST2), the white blood cell (WBC) count, and Gensini scores were compared among the groups. **Results** The HDL-C/ApoA1 ratio in the observation group was lower than that in the control group ($P < 0.05$), while the levels of MCP-1, CK-MB, CK, cTnI, hs-CRP and ST2 as well as the WBC count in the observation group were significantly higher than those in the control group ($P < 0.05$). The HDL-C/ApoA1 ratio in AMI and UAP patients was lower than that in SAP patients ($P < 0.05$), whereas the levels of MCP-1, CK-MB, CK, and cTnI in AMI and UAP patients were higher than those in SAP patients ($P < 0.05$). There was no different in the WBC count and the levels of hs-CRP and ST2 among AMI, UAP and SAP patients ($P > 0.05$). The HDL-C/ApoA1 ratio in patients with two and three branches involvement was lower than that in patients with one branch involvement ($P < 0.05$), while the levels of MCP-1, CK-MB, CK, and cTnI in patients with two and three branches involvement were higher than those in patients with one branch involvement ($P < 0.05$). There was no different in the WBC count and the levels of hs-CRP and ST2 among patients with different number of branches involved ($P > 0.05$). The HDL-C/ApoA1 ratio in patients with moderate and severe stenosis of the coronary artery was lower than that in patients with mild stenosis of the coronary artery ($P < 0.05$), whereas the levels of MCP-1, CK-MB, CK, cTnI, hs-CRP and ST2 as well as the WBC count in patients with moderate and severe stenosis of the coronary artery were higher than those in patients with mild stenosis of the coronary artery ($P < 0.05$). In the observation group, the HDL-C/ApoA1 ratio was negatively correlated with the levels of CK-MB, CK, cTnI, hs-CRP, and ST2, the WBC count, and Gensini scores ($P < 0.05$), while the level of MCP-1 was positively correlated with the levels of CK-MB, CK, cTnI, hs-CRP, and ST2, the WBC count, and Gensini scores ($P < 0.05$). **Conclusions** The HDL-C/ApoA1 ratio is decreased while the level of MCP-1 is increased among young and middle-aged patients with coronary heart disease. The HDL-C/ApoA1 ratio and the level of MCP-1 are associated with the type of diseases, number of branches of the coronary artery involved, and the disease severity. Meanwhile, the HDL-C/ApoA1 ratio and the level of MCP-1 are related to the inflammatory response in these patients.

Keywords: coronary heart disease; high-density lipoprotein cholesterol; apolipoprotein A1; monocyte chemoattractant protein-1; young and middle-aged; disease severity; inflammatory response

冠状动脉粥样硬化性心脏病(以下简称冠心病)是全世界发病率和病死率最高的疾病,常表现为胸痛、胸闷、心悸等典型症状^[1-3]。中青年冠心病患者更易发生无先兆症状的急性心肌梗死,病死率更高,预后更差,少部分患者甚至发生急性猝死^[4-6]。血清高密度脂蛋白胆固醇(high density lipoprotein cholesterol, HDL-C)可反映冠心病患者的风险^[7-9]。HDL-C水平越高,冠心病发生风险越低。载脂蛋白A1(apolipoprotein A1, ApoA1)主要存在于HDL-C中,可促进胆固醇转运,抑制粥样斑块形成,是冠

状动脉(以下简称冠脉)病变的预测因子^[10-12]。趋化因子在冠心病进展中扮演重要角色,其中单核细胞趋化蛋白-1(monocyte chemoattractant protein-1, MCP-1)可促使单核细胞迁入内皮下结缔组织,造成血管重塑和纤维化^[13]。动物实验证实MCP-1可促进冠脉硬化,但关于其与中青年冠心病关系的研究报道较少^[14]。基于此,本研究探讨HDL-C/ApoA1、MCP-1水平与中青年冠心病病变程度及炎症反应的相关性。

1 资料与方法

1.1 一般资料

选取 2021 年 10 月—2022 年 10 月在南通大学附属医院和如皋市人民医院就诊的中青年冠心病患者 130 例作为观察组, 其中稳定型心绞痛(stable angina pectoris, SAP)42 例, 不稳定型心绞痛(unstable angina pectoris, UAP)50 例, 急性心肌梗死(acute myocardial infarction, AMI)38 例; 病变支数: 单支病变 59 例, 双支病变 39 例, 三支病变 32 例(冠状动脉狭窄直径 \geq 50% 的病变所累及的主要冠状动脉的支数为病变支数, 累及左主干时以同时累及左前降支和左回旋支计算)。另取同期本院冠脉 CT 血管造影(CT angiography, CTA)或冠脉造影正常者 130 例作为对照组。观察组与对照组性别构成、年龄、体质量指数(body mass index, BMI)比较, 差异均无统计学意义($P>0.05$), 具有可比性。见表 1。本研究经医院医学伦理委员会批准, 患者及家属签署知情同意书。

表 1 观察组与对照组一般资料比较 ($n=130$)

组别	男/女/例	年龄/(岁, $\bar{x} \pm s$)	BMI/(kg/m ² , $\bar{x} \pm s$)
观察组	99/31	34.49 \pm 5.65	22.32 \pm 2.32
对照组	92/38	33.20 \pm 5.21	22.14 \pm 2.20
χ^2/t 值	0.967	1.914	0.642
P 值	0.326	0.057	0.522

1.2 纳入与排除标准

1.2.1 纳入标准 ①冠心病符合《实用内科学(第 16 版)》^[15]中的诊断标准, 且经冠脉造影确诊狭窄程度 \geq 50%; ②年龄 18~45 岁; ③初次治疗。

1.2.2 排除标准 ①合并有恶性肿瘤、自身免疫性疾病、急慢性感染等严重疾病; ②近 3 个月内有糖皮质激素、免疫抑制剂等药物使用史; ③有心脏手术史。

1.3 实验室方法

入院第 2 日清晨, 抽取患者肘静脉血 3 mL, 离心后提取上清液存储于无菌 EP 管中。采用 CHEMIX-180 型全自动生化分析仪(日本希森美康株式会社)测定肌酸激酶同工酶(creatinine kinase isoenzymes, CK-MB)、肌酸激酶(creatinine kinase, CK)、心肌肌钙蛋白 I(cardiac troponin I, cTn I), 超速离心结合 Abell-Levy-Brodie-Kendall 法检测 HDL-C。

采用酶联免疫试验检测 ApoA1、超敏 C 反应蛋白(hypersensitive C-reactive protein, hs-CRP)和生长刺激表达基因 2 蛋白(growth stimulating expressed gene 2, ST2)、单核细胞趋化蛋白-1、MCP-1, 试剂盒由中上海鑫乐生物科技公司提供, 严格参照试剂盒说明书进行操作。采用瑞典 HemoCue 公司细胞检测仪检测白细胞计数(white blood count, WBC)。

1.4 冠脉造影检查

采用 Gensini 评分系统评估冠脉病变程度: \leq 53 分为轻度, $>53 \sim 86$ 分为中度, >86 分为重度。其中轻度患者 46 例, 中度患者 54 例, 重度患者 30 例。

1.5 统计学方法

数据分析采用 SPSS 22.0 统计软件。计量资料以均数 \pm 标准差($\bar{x} \pm s$)表示, 比较用 t 检验或方差分析, 两两比较用 LSD- t 检验; 计数资料以构成比或率(%)表示, 比较用 χ^2 检验; 相关性分析用 Pearson 法。 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 观察组与对照组实验室检测指标比较

观察组与对照组 HDL-C/ApoA1、MCP-1、CK-MB、CK、cTn I、WBC、hs-CRP、ST2 水平比较, 经 t 检验, 差异均有统计学意义($P<0.05$); 观察组 HDL-C/ApoA1 低于对照组, MCP-1、CK-MB、CK、cTn I、WBC、hs-CRP、ST2 高于对照组。见表 2。

表 2 观察组与对照组实验室检测指标指标比较 ($n=130, \bar{x} \pm s$)

组别	HDL-C/ApoA1	MCP-1/(pg/mL)	CK-MB/(IU/L)	CK/(IU/L)	cTn I/(ng/mL)	WBC/($\times 10^9/L$)	hs-CRP/(mg/L)	ST2/(ng/mL)
观察组	0.72 \pm 0.15	144.40 \pm 22.54	20.20 \pm 6.81	94.45 \pm 14.42	3.10 \pm 0.79	6.60 \pm 1.32	4.10 \pm 1.00	71.19 \pm 12.23
对照组	0.88 \pm 0.18	103.34 \pm 21.80	7.03 \pm 1.43	44.40 \pm 8.92	0.70 \pm 0.22	5.04 \pm 1.40	1.80 \pm 0.67	19.10 \pm 9.92
t 值	-7.786	14.930	21.579	33.655	33.369	9.244	21.786	37.715
P 值	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

2.2 观察组不同疾病类型患者实验室检测指标比较

SAP、UAP、AMI患者的HDL-C/ApoA1、MCP-1、CK-MB、CK、cTn I水平比较,经方差分析,差异均有统计学意义($P < 0.05$);AMI和UAP患者的HDL-C/ApoA1低于SAP患者($P < 0.05$),MCP-1、CK-MB、CK、cTn I高于SAP患者($P < 0.05$)。SAP、UAP、AMI患者的WBC、hs-CRP、ST2比较,经方差分析,差异均无统计学意义($P > 0.05$)。见表3。

2.3 观察组不同病变支数患者实验室检测指标比较

单支、双支、三支病变患者的HDL-C/ApoA1、MCP-1、CK-MB、CK、cTn I比较,经方差分析,差异均有统计学意义($P < 0.05$);双支和三支病变患者的HDL-C/ApoA1低于单支病变患者($P < 0.05$),MCP-1、CK-MB、CK、cTn I高于单支病变患者($P < 0.05$)。不同病变支数患者的WBC、hs-CRP、ST2比较,经方差分析,差异均无统计学意义($P > 0.05$)。见表4。

表3 观察组不同疾病类型患者实验室检测指标比较 ($\bar{x} \pm s$)

疾病类型	<i>n</i>	HDL-C/ ApoA1	MCP-1/ (pg/mL)	CK-MB/ (IU/L)	CK/ (IU/L)	cTn I / (ng/mL)	WBC/ ($\times 10^9/L$)	hs-CRP/ (mg/L)	ST2/ (ng/mL)
SAP	42	0.83 ± 0.12	130.23 ± 21.10	17.73 ± 4.43	81.18 ± 11.50	2.04 ± 0.67	6.43 ± 1.04	4.03 ± 0.92	69.94 ± 11.30
UAP	50	0.71 ± 0.11 ^①	142.23 ± 23.54 ^①	20.11 ± 5.03 ^①	96.72 ± 12.27 ^①	3.17 ± 0.80 ^①	6.56 ± 1.12	4.22 ± 0.94	72.23 ± 12.50
AMI	38	0.58 ± 0.13 ^{①②}	162.95 ± 20.05 ^{①②}	23.05 ± 5.18 ^{①②}	106.13 ± 14.41 ^{①②}	4.18 ± 0.83 ^{①②}	6.84 ± 1.07	4.02 ± 0.91	71.20 ± 11.87
F值		43.780	22.906	11.819	39.800	77.427	1.492	0.683	0.42
P值		0.000	0.000	0.000	0.000	0.000	0.229	0.507	0.658

注:①与SAP比较 $P < 0.05$;②与UAP比较 $P < 0.05$ 。

表4 观察组不同病变支数患者实验室检测指标比较 ($\bar{x} \pm s$)

病变支数	<i>n</i>	HDL-C/ ApoA1	MCP-1/ (pg/mL)	CK-MB/ (IU/L)	CK/ (IU/L)	cTn I / (ng/mL)	WBC/ ($\times 10^9/L$)	hs-CRP/ (mg/L)	ST2/ (ng/mL)
单支	59	0.81 ± 0.11	132.27 ± 19.87	18.03 ± 4.80	79.98 ± 12.14	2.43 ± 0.89	6.81 ± 1.16	4.15 ± 0.98	72.28 ± 11.12
双支	39	0.70 ± 0.12 ^①	146.61 ± 20.80 ^①	21.12 ± 4.73 ^①	98.82 ± 13.04 ^①	3.15 ± 0.91 ^①	6.54 ± 1.09	4.05 ± 0.99	69.95 ± 10.43
三支	32	0.58 ± 0.10 ^{①②}	164.07 ± 22.54 ^{①②}	23.08 ± 4.42 ^{①②}	115.80 ± 12.70 ^{①②}	4.27 ± 0.96 ^{①②}	6.39 ± 1.12	4.07 ± 0.89	70.69 ± 12.08
F值		45.647	24.497	13.106	87.856	42.174	1.594	0.148	0.554
P值		0.000	0.000	0.000	0.000	0.000	0.207	0.863	0.576

注:①与单支比较 $P < 0.05$;②与双支比较 $P < 0.05$ 。

2.4 观察组不同严重程度患者实验室检测指标比较

不同严重程度患者HDL-C/ApoA1、MCP-1、CK-MB、CK、cTn I、WBC、hs-CRP、ST2比较,经方差分析,差异均

有统计学意义($P < 0.05$);中、重度患者的HDL-C/ApoA1低于轻度患者($P < 0.05$),MCP-1、CK-MB、CK、cTn I、WBC、hs-CRP、ST2高于轻度患者($P < 0.05$)。见表5。

表5 观察组不同严重程度患者实验室检测指标比较 ($\bar{x} \pm s$)

严重程度	<i>n</i>	HDL-C/ ApoA1	MCP-1/ (pg/mL)	CK-MB/ (IU/L)	CK/ (IU/L)	cTn I / (ng/mL)	WBC/ ($\times 10^9/L$)	hs-CRP/ (mg/L)	ST2/ (ng/mL)
轻度	46	0.83 ± 0.12	129.59 ± 19.10	17.54 ± 3.45	80.03 ± 11.20	2.54 ± 0.81	5.92 ± 1.08	3.56 ± 0.91	66.87 ± 9.95
中度	54	0.71 ± 0.11 ^①	148.82 ± 21.15 ^①	20.04 ± 4.00 ^①	97.18 ± 12.43 ^①	3.08 ± 0.88 ^①	6.71 ± 1.11 ^①	4.15 ± 0.94 ^①	71.14 ± 9.15 ^①
重度	30	0.57 ± 0.12 ^{①②}	158.97 ± 20.50 ^{①②}	24.57 ± 4.10 ^{①②}	111.65 ± 14.1 ^{①②}	3.99 ± 0.90 ^{①②}	7.44 ± 1.08 ^{①②}	4.84 ± 0.80 ^{①②}	77.90 ± 9.33 ^{①②}
F值		46.019	21.258	30.536	60.948	25.796	18.048	18.543	12.288
P值		0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

注:①与轻度比较 $P < 0.05$;②与中度比较 $P < 0.05$ 。

2.5 观察组 HDL-C/ApoA1、MCP-1 与其他实验室指标及 Gensini 评分的相关性

观察组 HDL-C/ApoA1 与 CK-MB、CK、cTn I、

WBC、hs-CRP、ST2 及 Gensini 评分均呈负相关($P < 0.05$);MCP-1 与 CK-MB、CK、cTn I、WBC、hs-CRP、ST2 及 Gensini 评分均呈正相关($P < 0.05$)。见表6。

表 6 观察组 HDL-C/ApoA1、MCP-1 与其他实验室指标及 Gensini 评分的相关性

指标	CK-MB		CK		cTn I		WBC		hs-CRP		ST2		Gensini 评分	
	r 值	P 值	r 值	P 值	r 值	P 值	r 值	P 值	r 值	P 值	r 值	P 值	r 值	P 值
HDL-C/ApoA1	-0.402	0.000	-0.387	0.021	-0.412	0.000	-0.332	0.027	-0.309	0.033	-0.314	0.029	-0.477	0.000
MCP-1	0.434	0.000	0.465	0.000	0.414	0.000	0.328	0.023	0.331	0.018	0.317	0.011	0.452	0.000

3 讨论

随着生活水平提高、饮食结构改变,冠心病的发病呈现年轻化趋势。青少年长期进食高油高脂的食物,血液黏度增加,易形成冠脉粥样斑块^[16-17]。此外,青少年吸烟率较高,容易影响机体脂类代谢,造成高脂血症,增加冠心病的发病风险^[18-19]。HDL-C 水平与冠心病的风险呈负相关,其水平上升每 1 mg/dL 可使冠心病发病率下降 2%~3%^[20]。HDL-C/ApoA1 可作为衡量 HDL 颗粒大小的指标,而 HDL 颗粒与 HDL 的功能密切相关。MCP-1 可迁入血管内膜下活化巨噬细胞,使其吞噬脂类,形成泡沫细胞及脂质池^[21-22]。

HDL 可逆转运细胞内胆固醇脂,抑制炎症因子的合成,促进血管内皮细胞的修复^[23-24]。ApoA1 存在于 HDL 中,可作用于动脉壁,促进胆固醇从动脉壁中流出,发挥抗动脉硬化的作用。炎症因子可刺激血管内皮导致血管内皮损伤,还可激活巨噬细胞使其变成泡沫细胞,加速冠脉粥样硬化的形成^[25-26]。本研究结果表明,观察组 HDL-C/ApoA1 低于对照组,而 MCP-1、CK-MB、CK、cTn I、WBC、hs-CRP、ST2 高于对照组,表明 HDL-C/ApoA1、MCP-1、CK-MB、CK、cTn I、WBC、hs-CRP、ST2 均与冠心病的发病密切相关。分析其原因为 ApoA1 是 HDL 主要蛋白质成分,其参与 HDL 形成,冠心病患者 ApoA1 水平常下降,导致 HDL 数量及质量下降,因此 HDL-C/ApoA1 降低;冠心病患者常存在慢性炎症,影响 ApoA1 合成和分泌,从而导致 ApoA1 水平下降, HDL-C/ApoA1 降低。当冠心病发生时,由于心肌细胞缺血及再灌注等因素刺激,CK-MB、CK、cTn I 升高,病变内皮细胞产生大量 MCP-1,吸引单核细胞进入血管壁,参与动脉粥样硬化发展。在冠心病发展中,血管壁炎症会导致 WBC、hs-CRP 升高。本研究结果表明,冠心病严重程度、病变血管数与 HDL-C/ApoA1 呈负相关,与 MCP-1、CK-MB、CK、cTn I 呈正相

关。HDL-C/ApoA1 反映抗动脉粥样硬化的潜能,当其显著降低时,冠脉病变程度加重。已有研究证实 HDL-C/ApoA1 可用于预测发生冠心病风险及冠脉病变严重程度^[27]。心肌梗死可导致大量心肌细胞坏死崩解,产生大量 cTn I,诱发强烈的炎症反应,故 MCP-1、CK-MB、CK 和 cTn I 水平明显升高。

Gensini 评分能综合反映冠状动脉的狭窄程度及病变范围,是一种经典的冠脉病变严重程度评分系统。本研究结果表明, HDL-C/ApoA1 与 CK-MB、CK、cTn I、WBC、hs-CRP、ST2 及 Gensini 评分呈负相关;可能是由于 HDL-C/ApoA1 升高可促进动脉粥样硬化病变逆转,降低心脏肌肉损伤和炎症的程度,从而减少心肌酶的释放,减轻炎症反应。本研究组中 MCP-1 与 CK-MB、CK、cTn I、WBC、hs-CRP、ST2 及 Gensini 评分呈正相关,表明 HDL-C/ApoA1、MCP-1 水平与冠心病病变程度存在一定相关性。既往多采用单一指标预测冠脉病变的程度,存在较大误差。本研究结果发现新的特异性预测因子,可为临床进一步研究提供线索。

综上所述,中青年冠心病患者 HDL-C/ApoA1 降低, MCP-1 升高。HDL-C/ApoA1、MCP-1 水平与疾病类型、病变支数及病情严重程度有关,与患者炎症反应有相关性。

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