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HDL-C 及其亚型与冠心病患者预后关系的相关性研究

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摘要 目的:探讨高密度脂蛋白胆固醇(HDL-C)及其亚型与冠心病患者预后的关系。**方法:**选取2012年6月~2015年12月在我院检查的371例疑似冠心病患者为研究对象,其中确诊为冠心病患者274例为观察组,冠状动脉检查正常者97例为对照组。对两组患者的血脂指标进行检测,同时分析各终点事件与血脂各指标之间的相关性,并采用COX回归分析探讨HDL-C及其亚型与冠心病患者预后的关系。**结果:**与正常组比较,冠心病患者总胆固醇、低密度脂蛋白胆固醇等指标显著升高,而高密度脂蛋白胆固醇及其亚型HDL2-C显著降低。这种改变随冠状动脉病变支数的增加而更加显著。COX回归分析显示HDL2-C亚型与患者源性死亡的发生风险存在一定的相关性。**结论:**HDL2-C亚型与冠心病的发生、发展,患者病变程度存在显著的相关性,可以用作对冠心病患者病情程度和终点事件预测的重要参考指标。

关键词:冠心病;预后;高密度脂蛋白胆固醇;亚型

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A Study on the Relationship between HDL-C Subtypes and Prognosis of Patients with Coronary Heart Disease

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ABSTRACT Objective: To investigate the relationship between high-density lipoprotein cholesterol (HDL-C) and its subtypes and the prognosis of patients with coronary heart disease. **Methods:** 371 suspected patients with coronary artery disease checked in our hospital from Jun 2012 to Dec 2015 were involved in this study. Among them, 274 cases of coronary heart disease patients were classified as observation group. Meanwhile, 97 patients with normal coronary artery were selected as control group. The blood lipid indexes of two groups were detected, and the relationship between HDL-C and its subtypes and the prognosis of patients with coronary heart disease was analyzed by COX regression analysis. **Results:** Compared with the control group, the levels of total cholesterol and low-density lipoprotein cholesterol in observation group were significantly increased, while HDL-cholesterol and its subtype HDL2-C were significantly decreased. This change is more significantly with the increased in the number of coronary lesions. The COX regression analysis showed that the HDL2-C subtypes had a certain correlation with the risk of cardiac death in patients and can be used to predict the risk of a cardiac event. **Conclusions:** The high density lipoprotein cholesterol subtypes has a significant correlation with the occurrence, development and pathological changes severity of the coronary heart disease. It can be used as an important reference indicator for predicting the extent of disease and the end events of the patients with coronary heart disease.

Key words: Coronary heart disease; Prognosis; High Density Lipoprotein; Subtypes

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前言

近年来,人口老龄化问题日益凸显,一些心血管疾病如冠心病、动脉粥样硬化等的发生率也呈现出逐渐增高的趋势^[1,2]。冠心病现在已经成为严重危害公众生命健康的疾病之一^[3,4]。研究表明血脂异常是导致心血管系统疾病尤其是冠心病的重要危险因素^[5,6]。其中,高密度脂蛋白胆固醇(HDL-C)降低可能是导致患者心血管疾病发生率升高的主要原因之一^[7,8]。HDL-C对心血管的保护作用机制相对复杂,至今尚未完全阐明。既往研究表明HDL-C对心血管的保护作用可能与胆固醇的逆转运

有关^[9,10]。目前,关于HDL-C及其亚型对冠心病患者不良事件的预测价值尚不明确,且已有研究显示不同亚型的高密度脂蛋白可能具有完全相反的作用,部分具有抑制动脉粥样硬化的作用,而另一部分则会这种作用产生抵消^[11,12]。因此,本研究主要探讨了HDL-C及其亚型与冠心病的相关性及其对患者预后的预测价值,以期对冠心病的临床治疗提供线索和参考。

1 资料与方法

1.1 资料来源

选取2012年6月~2015年12月在我院接受冠状动脉造影检查的患者371例为研究对象。其中,确诊为冠心病患者274例为观察组,冠状动脉检查正常者97例为对照组。冠心病诊断符合参考文献^[1]诊断标准。排除急性心肌梗死、不稳定型心

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绞痛、心力衰竭、肾功能不全、恶性肿瘤等并发有其他疾病患者。两组患者年龄、性别、BMI 指数等一般资料比较差异无统计学意义($P<0.05$),具有可比性,见表 1。

表 1 两组患者的一般资料比较

Table 1 Comparison of the general information between two groups of patients

Groups	Amount (n)	Ages (Years)	Gender (male/female)	BMI (kg/m ²)
Control Group	97	54.06± 11.09	56/41	26.15± 2.58
Observation Group	274	55.34± 11.61	163/111	26.40± 2.61

1.2 检查方法

所有患者入院后均详细记录既往病史,并于次日清晨空腹采集肘静脉血,加入 EDTA 抗凝后离心,分离血浆,对血脂常规指标及 HDL-C 亚型进行检测。对总胆固醇 (TC) 及三酰甘油 (TG) 采用酶法进行检测,对 HDL-C 及低密度脂蛋白胆固醇 (LDL-C) 采用均相法检测,对载脂蛋白 A1(ApoA1)及载脂蛋白 B(ApoB)采用免疫投射比浊法检测,使用 PEG20000 沉淀法对 HDL 亚型进行测定,并通过换算计算 HDL 各亚型含量。

1.3 统计学方法

利用 SPSS 17.0 统计分析软件对结果进行分析,正态分布的计量资料采用均值± 标准差($\bar{x}\pm s$)表示,采用独立样本 t 检

验,非正态分布计量资料以 $M(P_{25}, P_{75})$ 表示,采用非参数秩和检验,多组数据间比较使用单因素方差分析,并使用 LSD-t 检验进行多重比较;以 Cox 回归对 HDL 亚型对冠心病患者终点事件发生风险进行预测,以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组患者血脂指标比较

与对照组比较,观察组 TC 及 LDL-C 显著升高,而 HDL-C、HDL2-C、HDL2-C/HD-C 及 ApoA1 显著降低,差异均有统计学意义($P<0.05$),见表 2。

表 2 两组患者血脂指标比较

Table 2 Comparison of the blood lipid indexes between the two groups

Groups	Amount (n)	TG (mmol/L)	TC (mmol/L)	LDL-C (mmol/L)	HDL-C (mmol/L)	HDL3-C (mmol/L)
Cotrol Group	97	1.72(1.51, 1.94)	4.06(3.24, 4.62)	2.28± 0.39	1.04(0.88, 1.21)	0.51± 0.10
Observation Group	274	1.80(1.51, 2.04)	4.25(3.44, 5.18) **	2.48± 0.43**	0.84(0.73, 0.96) **	0.51± 0.11

Groups	Amount (n)	HDL2-C (mmol/L)	HDL2-C/HDL	ApoA1 (g/L)	ApoB (g/L)
Control Group	97	0.53(0.35, 0.70)	0.50(0.41, 0.58)	1.39(1.25, 1.57)	0.77(0.67, 0.89)
Observation Group	274	0.33(0.27, 0.41)**	0.40(0.34, 0.46) **	1.37(1.21, 1.49)*	0.80(0.63, 0.97)

Note: * $P<0.05$, ** $P<0.01$ compared with control group.

2.2 冠状动脉病变支数与血脂各指标之间的关系

根据患者冠状动脉病变支数将冠心病患者进一步分为单支病变、双支病变及多支病变组。三组患者 TG、HDL3-C 及 ApoB 比较差异无统计学意义($P>0.05$),其余各血脂指标比较差

异均有统计学意义($P<0.05$)。随着患者病变支数的增加,患者 TC 及 LDL-C 指标增高,而 HDL-C、HDL2-C、HDL2-C/HDL-C 及 ApoA1 等指标则降低,见表 3。

表 3 冠状动脉病变支数与血脂各指标之间的关系

Table 3 The relationship between the number of coronary artery lesions and the indicators of blood lipids

Groups	Amount (n)	TG (mmol/L)	TC (mmol/L)	LDL-C (mmol/L)	HDL-C (mmol/L)	HDL3-C (mmol/L)
Single Vessel	126	1.76(1.49, 2.03)	4.04(3.29, 4.94)	2.34± 0.39	0.90(0.79, 1.02)	0.51± 0.10
Double Vessel	93	1.80(1.56, 2.04)	4.46(3.45, 5.25)	2.51± 0.40	0.81(0.76, 0.93)	0.50± 0.11
Multiple Vessel	55	1.84(1.51, 2.10)	4.68(3.82, 5.52)**	2.75± 0.42**	0.72(0.62, 0.82) **	0.49± 0.12

Groups	Amount (n)	HDL2-C (mmol/L)	HDL2-C/HDL-C	ApoA1 (g/L)	ApoB (g/L)
Single Vessel	126	0.40(0.32, 0.48)	0.44(0.37, 0.48)	1.43(1.27, 1.54)	0.79(0.63, 0.97)
Double Vessel	93	0.32(0.27, 0.37)	0.38(0.34, 0.44)	1.35(1.20, 1.46)	0.80(0.64, 0.95)
Multiple Vessel	55	0.22(0.18, 0.28)**	0.32(0.25, 0.38)**	1.27(1.14, 1.40)**	0.81(0.64, 1.01)

Note:** $P<0.01$.

2.3 HDL 及其亚型对冠心病患者终点预测的价值

对 274 例冠心病患者进行了平均时间为 20(17,22)个月的随访,其中发生不良事件的患者 119 人,未发生不良事件的患

者 155 人。根据患者不良事件的发生情况,将患者分为无事件组和有事件组。有事件组 HDL-C 和 HDL2-C 较无事件组低,见表 4。

表 4 冠心病患者事件发生情况基线参数比较

Table 4 Comparison of the baseline parameters between coronary heart disease patients with and without event

Groups	Amount (n)	TG (mmol/L)	TC (mmol/L)	LDL-C (mmol/L)	HDL-C (mmol/L)	HDL3-C (mmol/L)
No Event Group	155	1.84(1.54, 2.09)	4.23 (3.45, 5.20)	2.45± 0.42	0.86 (0.74, 0.98)	0.51± 0.11
Event Group	119	1.74 (1.46, 1.99)	4.26 (3.44, 5.09)	2.54± 0.44	0.81 (0.73, 0.91)*	0.50± 0.11
Groups	Amount (n)	HDL2-C (mmol/L)	HDL2-C/HDL-C (%)	ApoA1 (g/L)	ApoB (g/L)	
No Event Group	155	0.34 (0.28, 0.43)	0.41 (0.35, 0.46)	1.39 (1.21, 1.49)	0.75 (0.63, 0.96)	
Event Group	119	0.31 (0.24, 0.39)*	0.39 (0.33, 0.45)	1.36 (1.20, 1.49)	0.85 (0.68, 0.98)	

Note:* $P<0.05$.

2.4 HDL-C 及 HDL2-C 对冠心病患者终点事件发生风险的预测价值

将 HDL-C 及 HDL2-C 按连续变量纳入 COX 回归模型,同时纳入的协变量指标还包括年龄、性别(男 =1,女 =0)、BMI 指数、吸烟状况(是 =1,否 =0)、饮酒状况(每周 1 次 =1,不常饮酒

=0)、高血压(是 =1,否 =0)、糖尿病(是 =1,否 =0)、LDL-C。对冠心病患者终点总事件以及心源性死亡进行预测,结果显示 HDL-C 对冠心病各事件的终点没有明确的预测价值,而低水平的 HDL2-C 及高血压对冠心病患者心源性死亡的发生风险具有一定的预测价值。结果见表 5、6。

表 5 对冠心病患者终点总事件预测作用的 COX 回归分析

Table 5 COX Regression Analysis on the Prediction of the Total Event of Patients with Coronary Heart Disease

Index	B	SE	HR	95%CI	P
HDL2-C	-0.752	2.163	0.472	0.007~32.737	0.827
HDL-C	-0.200	0.831	0.819	0.161~4.179	0.810
LDL-C	-0.013	0.228	0.988	0.631~1.545	0.956
Age	0.014	0.017	1.014	0.981~1.048	0.424
Gender	-0.367	0.190	0.693	0.477~1.006	0.053
BMI	-0.021	0.036	0.979	0.913~1.050	0.549
Hypertension	0.234	0.206	1.264	0.844~1.892	0.255
Diabetes	0.023	0.238	1.023	0.641~1.633	0.924
Smoking	0.070	0.213	1.072	0.707~1.627	0.742
Alcohol Drinking	-0.223	0.289	0.800	0.454~1.409	0.440

表 6 对冠心病患者心源性死亡预测作用的 COX 回归分析

Table 6 COX Regression Analysis on Predicting Cardiac Death in Patients with Coronary Heart Disease

Index	B	SE	HR	95%CI	P
HDL2-C	-19.564	8.466	0.000	0.000~0.51	0.021
HDL-C	-1.345	2.459	0.260	0.002~21.254	0.584
LDL-C	0.182	0.668	1.200	0.324~4.445	0.785
Age	0.040	0.070	1.041	0.907~1.195	0.565
Gender	-0.320	0.678	0.267	0.71~1.009	0.052
BMI	-0.118	0.112	0.889	0.714~1.106	0.290
Hypertension	2.081	0.836	8.009	1.555~41.239	0.013
Diabetes	-0.542	0.748	0.582	0.134~2.522	0.469
Smoking	0.940	0.624	2.560	0.753~8.704	0.132
Alcohol Drinking	0.680	0.673	1.975	0.528~7.380	0.312

3 讨论

近年来,随着人们生活习惯的改变及生活水平的提高,人们的平均寿命得以显著延长,人口老龄化现象愈加明显,冠心病及其所引发的不良后果对人民生命健康的威胁也越来越受到关注^[13,14]。虽然目前冠心病的诊断及治疗都已相对规范,但及时对患者不良事件发生风险进行预测,降低患者不良事件发生率,从而延长患者生命仍然十分必要^[15,16]。目前大量临床研究已经证实 LDL-C 及 HDL-C 在冠心病的发生中扮演者十分重要的角色。其中, HDL-C 对血管有直接的保护作用,由于 HDL-C 能够促进患者动脉粥样斑块的消退,其与冠心病之间存在负相关的关系。一些研究甚至显示与 LDL-C 相比, HDL-C 对冠心病发生率的预测作用更强^[17-20]。

本研究结果显示冠心病患者的血脂指标与正常人相比存在一定的差异,冠心病患者总胆固醇、LDL-C 升高而 HDL-C 出现降低。随着患者病变程度的增加,患者的 LDL-C 的升高及 HDL-C 分别存在着升高和降低的趋势。不同病变支数的患者的血脂特点也显示出了相似的规律,患者 TC、LDL-C 越高以及 HDL-C 越低,罹患冠心病的风险越高,病变的程度也越严重。对冠心病患者不良事件发生的基线参数进行分析结果显示发生不良事件的患者在 HDL-C 及 HDL2-C 两方面存在统计学差异,其他方面的差异不显著。这可能的原因是由于冠心病患者长期处于炎症状态, HDL-C 水平因此降低,进而削弱了患者心血管系统的保护功能,进而引发更为严重的循环系统疾病。

对冠心病患者终点预测的回归分析结果显示 HDL-C 无法对患者各个终点事件进行准确、有效的预测,而 HDL2-C 能够对患者心源性死亡实现较好的预测效果,这说明以 HDL2-C 来对冠心病患者进行评价可能得到更准确的结果。此外,一些其他研究同时显示亚型中 HDL2-C 水平的显著降低,可能是 HDL-C 水平显著降低的根本原因,这也是导致患者 TC/HDL-C 水平升高的根本因素。因此,在使用 TC、LDL-C 及 HDL-C 对患者血脂状况进行评估的同时增加临床实验室对血清 HDL-C 各亚型组成的检测可以为患者血脂状况以及心血管系统病变程度的准确预测和评估提供更有效的补充。而通过药物或饮食改变患者 HDL-C 亚型分布,增加 HDL2-C 水平或许对于患者心血管疾病的治疗及预防具有非常重要的意义。

综上所述, HDL2-C 亚型与冠心病的发生、发展,患者病变程度存在显著的相关性,可以用作对冠心病患者病情程度和终点事件预测的重要指标之一,提高患者 HDL2-C 水平对于延缓患者动脉粥样硬化、降低冠心病患者不良事件发生率具有重要的临床意义。

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