



· 论著 ·

脂蛋白相关磷脂酶 A2 与冠心病患者踝臂指数、心率变异性的相关性研究

刘向阳, 李爱华, 唐良秋

【摘要】 背景 踝臂指数 (ABI) 可预测冠状动脉狭窄, 心率变异性 (HRV) 降低与冠心病 (CHD) 的进展有关, 脂蛋白相关磷脂酶 A2 (Lp-PLA2) 是 CHD 患者冠状动脉狭窄的危险因素, 但三者之间的关系目前尚不明确。目的 分析 Lp-PLA2 与 CHD 患者 ABI、HRV 的相关性, 并分析 Lp-PLA2 对 CHD 患者 ABI 及 HRV 异常的预测价值。方法 选取 2016 年 4 月—2019 年 1 月汕头大学附属粤北人民医院心血管内科确诊的非 CHD 患者 292 例作为 A 组, 同期确诊的 CHD 患者 389 例作为 B 组。比较两组患者一般资料、实验室检查指标、血脂指标及 ABI、HRV; 变量间的相关性分析采用 Pearson 偏相关及多元线性回归分析; 绘制 ROC 曲线以评价 Lp-PLA2 对 CHD 患者 ABI 及 HRV 异常的预测价值。结果 (1) 两组患者高血压病史、体质指数 (BMI)、三酰甘油 (TG)、载脂蛋白 B (ApoB) 比较, 差异无统计学意义 ($P>0.05$); B 组患者年龄、有 2 型糖尿病病史者所占比例、同型半胱氨酸 (Hcy)、Lp-PLA2、糖化血红蛋白 (HbA_{1c})、超敏 C 反应蛋白 (hs-CRP)、脂蛋白 a [LP(a)] 高于 A 组, 总胆固醇 (TC)、载脂蛋白 A (ApoA)、高密度脂蛋白胆固醇 (HDL-C)、低密度脂蛋白胆固醇 (LDL-C)、ABI 及全部窦性心搏 RR 间期的标准差 (SDNN) 低于 A 组 ($P<0.05$)。 (2) Lp-PLA2 未进入多元线性回归方程。Pearson 偏相关分析结果显示, ABI 与 CHD ($r=-0.147$)、Hcy ($r=-0.082$) 呈负相关, 与 BMI ($r=0.119$)、SDNN ($r=0.157$) 呈正相关 ($P<0.05$)。多元线性回归分析结果显示, ABI 与 CHD ($\beta=-0.50$) 和 Hcy ($\beta=-0.01$) 呈负相关, 与 BMI ($\beta=0.004$) 和 SDNN ($\beta=0.001$) 呈正相关 ($P<0.05$)。 (3) Pearson 偏相关分析结果显示, SDNN 与 Lp-PLA2 ($r=-0.098$)、hs-CRP ($r=-0.123$) 呈负相关 ($P<0.05$)。多元线性回归分析结果显示, SDNN 与 CHD 患者 Lp-PLA2 ($\beta=-0.040$)、hs-CRP ($\beta=-4.388$) 负相关, 与 ABI ($\beta=43.301$) 呈正相关 ($P<0.05$)。 (4) ROC 曲线显示, Lp-PLA2 预测 CHD 患者 ABI 异常的曲线下面积 (AUC) 为 0.583 [95%CI (0.480, 0.687)], 灵敏度为 0.84、特异度为 0.38; Lp-PLA2 预测 CHD 患者 SDNN 异常的 AUC 为 0.656 [95%CI (0.600, 0.712)], 灵敏度为 0.76, 特异度为 0.48。结论 CHD 患者 Lp-PLA2 升高, ABI、HRV 降低; Lp-PLA2 与 CHD 患者 HRV 呈负相关且对 CHD 患者 HRV 异常有一定的预测价值, 但其与 CHD 患者 ABI 无关, 而 ABI 与 CHD 患者 HRV 呈正相关。

【关键词】 冠心病; 脂蛋白相关磷脂酶 A2; 踝臂指数; 心率变异性

【中图分类号】 R 541.4 **【文献标识码】** A DOI: 10.3969/j.issn.1008-5971.2020.03.010

刘向阳, 李爱华, 唐良秋. 脂蛋白相关磷脂酶 A2 与冠心病患者踝臂指数、心率变异性的相关性研究 [J]. 实用心脑血管病杂志, 2020, 28 (3): 44-50. [www.syxnf.net]

LIU X Y, LI A H, TANG L Q. Correlations of lipoprotein-associated phospholipase A2 with ankle-brachial index and heart rate variability in patients with coronary heart disease [J]. Practical Journal of Cardiac Cerebral Pneumal and Vascular Disease, 2020, 28 (3): 44-50.

Correlations of Lipoprotein-associated Phospholipase A2 with Ankle-brachial Index and Heart Rate Variability in Patients with Coronary Heart Disease

LIU Xiangyang, LI Aihua, TANG Liangqiu

Department of Cardiovascular Medicine, North Guangdong People's Hospital Affiliated to Shantou University, Shaoguan 512026, China

Corresponding author: TANG Liangqiu, E-mail: TLQ_55048@sina.com

【Abstract】 **Background** Ankle-brachial index (ABI) can predict coronary artery stenosis, decrease of heart rate variability (HRV) is associated with progress of coronary heart disease (CHD), lipoprotein-associated phospholipase A2 (Lp-PLA2) is the risk factor of coronary artery stenosis in patients with CHD, however, interrelationship of the above three is not yet clear. **Objective** To analyze the correlations of Lp-PLA2 with ABI and HRV in patients with CHD, and to analyze

基金项目: 广东省韶关市医药卫生科研计划项目 (Y17015); 广东省韶关市科技局计划项目 (2017CX/K011)

512026 广东省韶关市, 汕头大学附属粤北人民医院心血管内科

通信作者: 唐良秋, E-mail: TLQ_55048@sina.com

the predictive value of Lp-PLA2 on ABI abnormality as well as HRV abnormality in patients with CHD. **Methods** From April 2016 to January 2019, 292 non-CHD patients were selected as A group in the Department of Cardiovascular Medicine, North Guangdong People's Hospital Affiliated to Shantou University, meanwhile 389 patients with CHD were selected as B group. Comparison of general information, laboratory examination results, blood lipid parameters, ABI and HRV was conducted between the two groups; Pearson partial correlation analysis and multiple linear regression analysis were used to analyze the correlations between variables, moreover ROC curve was drawn to evaluate the predictive value of Lp-PLA2 on ABI abnormality as well as HRV abnormality in patients with CHD. **Results** (1) No statistically significant difference of history of hypertension, BMI, TG or ApoB was found between the two groups ($P>0.05$); age, proportion of patients with history of diabetes, Hcy, Lp-PLA2, HbA_{1c}, hs-CRP and Lp (a) in B group were statistically significantly higher than those in A group, while TC, ApoA, HDL-C, LDL-C, ABI and SDNN in B group were statistically significantly lower than those in A group ($P<0.05$). (2) Lp-PLA2 did not enter into the multiple linear regression analysis. Pearson partial correlation analysis results showed that, ABI was negatively correlated with CHD ($r=-0.147$) and Hcy ($r=-0.082$), respectively, but was positively correlated with BMI ($r=0.119$) and SDNN ($r=0.157$), respectively ($P<0.05$). Multiple linear regression analysis results showed that, ABI was negatively correlated with CHD ($\beta=-0.50$) and Hcy ($\beta=-0.01$), respectively, but was positively correlated with BMI ($\beta=0.004$) and SDNN ($\beta=0.001$), respectively ($P<0.05$). (3) Pearson partial correlation analysis results showed that, SDNN was negatively correlated with Lp-PLA2 ($r=-0.098$) and hs-CRP ($r=-0.123$), respectively ($P<0.05$). Multiple linear regression analysis results showed that, SDNN was negatively correlated with Lp-PLA2 ($\beta=-0.040$) and hs-CRP ($\beta=-4.388$), respectively, but was positively correlated with ABI ($\beta=43.301$) ($P<0.05$). (4) ROC curves indicated that, AUC, sensitivity and specificity of Lp-PLA2 in predicting ABI abnormality in patients with CHD was 0.583 [95%CI (0.480, 0.687)], 0.84 and 0.38, respectively; AUC, sensitivity and specificity of Lp-PLA2 in predicting SDNN abnormality in patients with CHD was 0.656 [95%CI (0.600, 0.712)], 0.76 and 0.48, respectively. **Conclusion** Lp-PLA2 increases but ABI and HRV decrease in patients with CHD; Lp-PLA2 is negatively correlated with HRV and it has predictive value on HRV abnormality in patients with CHD to some extent, however Lp-PLA2 is not significantly correlated with ABI in patients with CHD, but there is positive correlation between ABI and HRV.

【Key words】 Coronary heart disease; Lipoprotein-associated phospholipase A2; Ankle-brachial Index; Heart rate variability

受环境变化、不良饮食习惯及社会压力增加等影响,近年来我国冠心病(coronary heart disease, CHD)等慢性疾病的发病率逐年上升。缺血性心血管疾病患者易并发外周动脉疾病,而踝臂指数(ankle-brachial index, ABI)可筛查无症状的下肢动脉狭窄^[1],预测冠状动脉左前降支狭窄^[2]。心率变异性(heart rate variability, HRV)是判断心脏自主神经功能的定量指标,研究表明,HRV正常的人群CHD发生风险较低^[3],而HRV降低与CHD的进展有关^[4]。近年研究表明,一种特异性新型血管炎性标志物—脂蛋白相关磷脂酶A2(lipoprotein-associated phospholipase A2, Lp-PLA2)升高会加快冠状动脉粥样硬化进展,并可预测CHD患者冠状动脉狭窄程度^[5],也可判断CHD患者预后^[6-8]。郭攸胜等^[9]研究发现,ABI、Lp-PLA2与CHD有关,但其未评价前两者间的关系。张伟伟^[10]发现,长程HRV与Lp-PLA2、冠状动脉病变有关,但其未明确Lp-PLA2对HRV的预测价值。本研究旨在分析Lp-PLA2与CHD患者ABI、HRV的相关性,并分析Lp-PLA2对CHD患者ABI及HRV异常的预测价值,现报道如下。

1 对象与方法

1.1 研究对象 回顾性分析2016年4月—2019年1月汕头大学附属粤北人民医院心血管内科确诊的非CHD患者292例作为A组,均经冠状动脉造影或心脏CT血管造影检查证实冠状动脉内径狭窄率 $<50\%$;选取同期确诊为CHD的患者389例作为B组,均经冠状动脉造影或心脏CT血管造影检查证实冠状动脉内径狭窄率 $\geq 50\%$ 。排除标准:(1)年龄 >80 岁;(2)合并严重心、肝、肾功能不全者;(3)伴有严重焦虑者;(4)合并急慢性感染、恶性肿瘤及严重动脉中层钙化者;(5)合并锁骨下动脉狭窄或闭塞、远端腹主动脉或髂总动脉狭窄或闭塞、外周静脉血栓或肢体缺失者。本研究经汕头大学附属粤北人民医院医学伦理委员会审核批准,所有患者签署知情同意书。

1.2 观察指标

1.2.1 一般资料 通过医院信息系统收集所有患者一般资料,包括年龄、高血压病史、2型糖尿病病史、体质指数(BMI)等。

1.2.2 实验室检查指标 记录所有患者同型半胱氨酸(Hcy)、Lp-PLA2、糖化血红蛋白(HbA_{1c})、超敏C反应蛋白(hs-CRP)、血脂指标{包括总胆固醇(TC)、

三酰甘油(TG)、脂蛋白a[LP(a)],载脂蛋白A(ApoA)、载脂蛋白B(ApoB)、高密度脂蛋白胆固醇(HDL-C)、低密度脂蛋白胆固醇(LDL-C)}。

1.2.3 ABI 采用科林公司生产的VP-1000全自动动脉硬化测量仪检测所有患者踝部血压和上臂血压并计算左、右ABI,取两者最低值。

1.2.4 HRV 采用美林公司生产的三通道固态式DCG监测系统监测所有患者24h动态心电图后做时域分析,取全部窦性心搏RR间期的标准差(SDNN)作为HRV的衡量指标。

1.3 统计学方法 采用SPSS 22.0统计学软件进行数据分析,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;计数资料分析采用 χ^2 检验;相关性分析采用Pearson偏相关性分析及多元线性回归分析, $\alpha_{入}=0.05$, $\alpha_{出}=0.10$;绘制受试者工作特征曲线(ROC曲线)以评价Lp-PLA2预测ABI、HRV异常的诊断价值。以 $P<0.05$ 为差异有统计学意义。

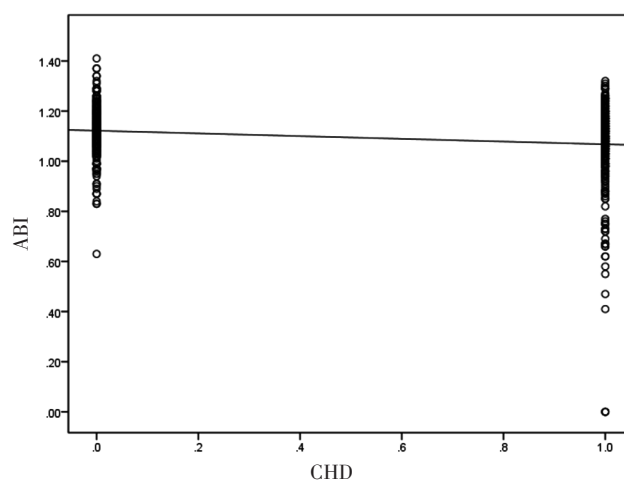
2 结果

2.1 两组患者一般资料、实验室检查指标及ABI、SDNN比较 两组患者高血压病史、BMI、TG、ApoB比较,差异无统计学意义($P>0.05$);B组患者年龄、有2型糖尿病病史者所占比例、Hcy、Lp-PLA2、HbA_{1c}、hs-CRP、Lp(a)高于A组,TC、ApoA、HDL-C、LDL-C、ABI及SDNN低于A组,差异有统计学意义($P<0.05$,见表1)。

2.2 ABI与一般资料、实验室检查指标及SDNN的相关性及多元线性回归分析 Lp-PLA2未进入多元线性回归方程。Pearson偏相关分析结果显示,ABI与CHD呈负相关($r=-0.147$, $P<0.01$,见图1),与Hcy呈负相关($r=-0.082$, $P=0.045$,见图2),与BMI呈正相

关($r=0.119$, $P=0.004$,见图3),与SDNN呈正相关($r=0.157$, $P<0.01$,见图4)。以ABI(y)为因变量,以CHD(X1)、Hcy(X2)、BMI(X3)、SDNN(X4)为自变量进行多元线性回归分析(回归方程为 $y=0.958-0.173X1-0.081X2+0.102X3+0.179X4$),结果显示,ABI与CHD、Hcy呈负相关,与BMI及SDNN呈正相关($P<0.05$,见表2)。

2.3 SDNN与一般资料、实验室检查指标及ABI相关性 及多元线性回归分析 Pearson偏相关分析结果显示,SDNN与Lp-PLA2呈负相关($r=-0.098$, $P=0.017$,见图5),与hs-CRP呈负相关($r=-0.123$, $a=0.003$,见图6)。以SDNN为因变量(y),以Lp-PLA2(X1)、hs-CRP(X2)、ABI(X3)为自变量进行多元线性回归分析(回归方程为 $y=83.202-0.122X1-$



注:ABI=踝臂指数,CHD=冠心病

图1 ABI与CHD相关性的散点图

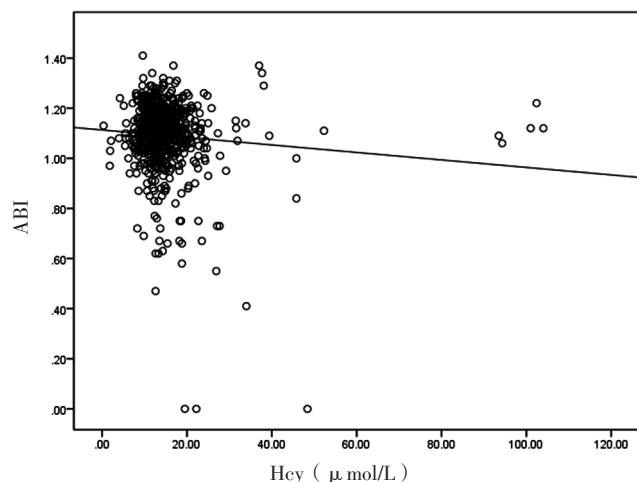
Figure 1 Scatter plot for correlation between ABI and CHD

表1 两组患者一般资料、实验室检查指标及ABI、SDNN比较

Table 1 Comparison of general information, laboratory examination results, ABI and SDNN between the two groups

组别	例数	年龄 ($\bar{x} \pm s$, 岁)	高血压病史 [n (%)]	2型糖尿病病 史[n (%)]	BMI ($\bar{x} \pm s$, kg/m ²)	Hcy ($\bar{x} \pm s$, μmol/l)	Lp-PLA2 ($\bar{x} \pm s$, g/L)	HbA _{1c} ($\bar{x} \pm s$, %)	hs-CRP ($\bar{x} \pm s$, g/L)
A组	292	58.9 ± 11.0	209 (71.6)	48 (16.4)	24.0 ± 3.5	14.02 ± 10.11	213.1 ± 104.8	5.80 ± 0.99	0.35 ± 0.60
B组	389	63.3 ± 9.9	295 (75.8)	139 (35.7)	24.6 ± 3.4	15.44 ± 8.23	258.2 ± 125.5	6.24 ± 1.28	0.72 ± 1.66
$t(\chi^2)$ 值		-5.487	-1.245 ^a	-5.915 ^a	-1.922	-2.014	-5.042	-5.046	-3.970
P值		<0.01	0.214	<0.01	0.055	0.044	<0.01	<0.01	<0.01
组别	TC ($\bar{x} \pm s$, mmol/L)	TG ($\bar{x} \pm s$, mmol/L)	Lp(a) ($\bar{x} \pm s$, mg/L)	ApoA ($\bar{x} \pm s$, g/L)	ApoB ($\bar{x} \pm s$, g/L)	HDL-C ($\bar{x} \pm s$, mmol/L)	LDL-C ($\bar{x} \pm s$, mmol/L)	ABI ($\bar{x} \pm s$)	SDNN ($\bar{x} \pm s$)
A组	4.86 ± 1.04	1.54 ± 0.93	16.5 ± 18.2	1.47 ± 0.47	0.88 ± 0.21	1.24 ± 0.30	3.09 ± 0.85	1.12 ± 0.10	122.20 ± 37.92
B组	4.64 ± 1.06	1.65 ± 1.31	21.6 ± 22.2	1.37 ± 0.30	0.88 ± 0.21	1.14 ± 0.28	2.95 ± 0.89	1.07 ± 0.17	115.08 ± 40.38
$t(\chi^2)$ 值	2.706	-1.264	-3.185	3.202	0.230	4.367	1.988	5.367	2.338
P值	0.007	0.228	0.002	0.001	0.818	<0.01	0.047	<0.01	0.019

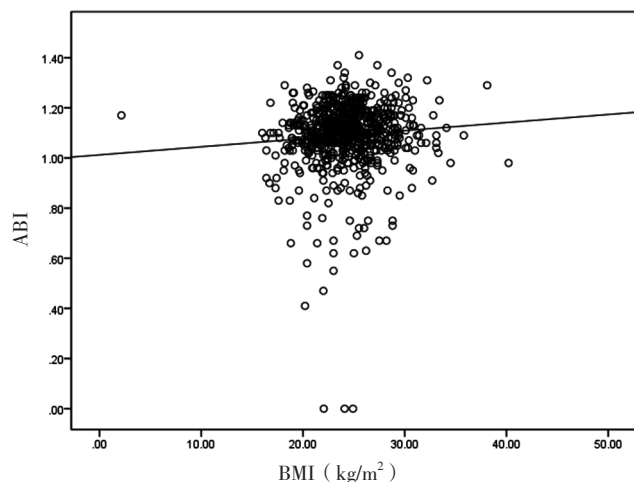
注: BMI= 体质指数, Hcy= 同型半胱氨酸, Lp-PLA2= 脂蛋白相关磷脂酶A2, HbA_{1c}= 糖化血红蛋白, hs-CRP= 超敏C反应蛋白, TC= 总胆固醇, TG= 三酰甘油, LP(a)= 脂蛋白a, ApoA= 载脂蛋白A, ApoB= 载脂蛋白B, HDL-C= 高密度脂蛋白胆固醇, LDL-C= 低密度脂蛋白胆固醇, ABI= 踝臂指数, SDNN= 窦性心搏RR间期的标准差; A组为非CHD患者, B组为CHD患者; ^a为 χ^2 值



注: Hcy= 同型半胱氨酸

图2 ABI与CHD患者Hcy相关性的散点图

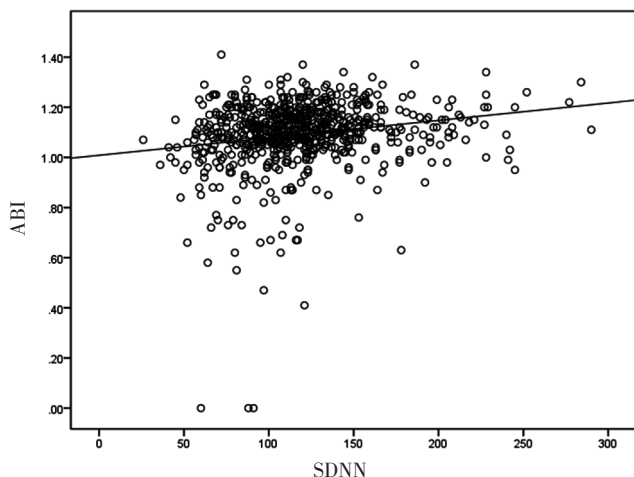
Figure 2 Scatter plot for correlation between ABI and Hcy in patients with CHD



注: BMI= 体质指数

图3 ABI与CHD患者BMI相关性的散点图

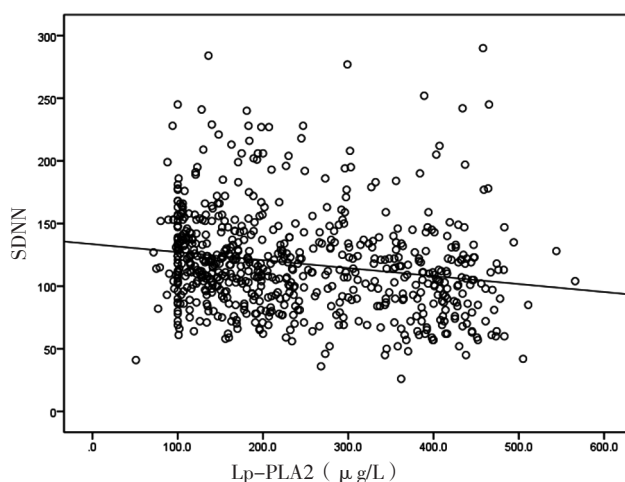
Figure 3 Scatter plot for correlation between ABI and BMI in patients with CHD



注: SDNN= 窦性心搏RR间期的标准差

图4 ABI与CAD患者SDNN相关性的散点图

Figure 4 Scatter plot for correlation between ABI and SDNN in patients with CHD



注: Lp-PLA2= 脂蛋白相关磷脂酶A2

图5 SDNN与CHD患者Lp-PLA2相关性的散点图

Figure 5 Scatter plot for correlation between SDNN and LP-PLA2 in patients with CHD

0.151X₂+0.159X₃), 结果显示, SDNN与CHD患者Lp-PLA2、hs-CRP负相关, 与ABI呈正相关($P<0.05$, 见表3)。

表2 ABI与CHD、BMI、Hcy、SDNN的多元线性回归分析

Table 2 Multiple linear regression analysis on correlations of ABI with CHD, BMI, Hcy and SDNN

变量	B	SE	β	t值	P值
常量	0.958	0.043	—	22.380	<0.01
CHD	-0.050	0.011	-0.173	-4.635	<0.01
BMI	0.004	0.002	0.102	2.739	0.006
Hcy	-0.001	0.001	-0.081	-2.170	0.030
SDNN	0.001	0.000	0.179	4.830	<0.01

注: “—”为无此项数据

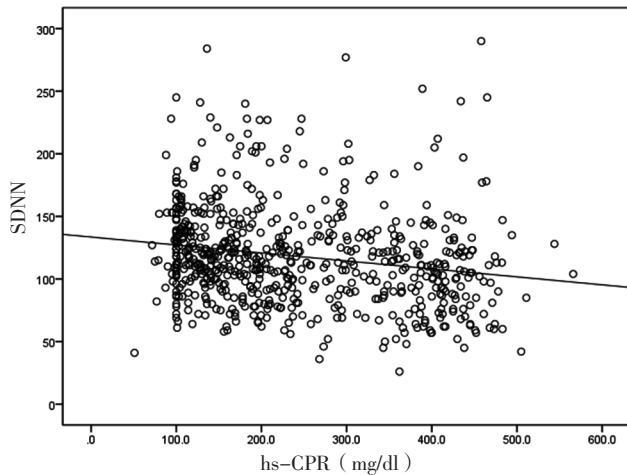
表3 SDNN与CHD患者Lp-PLA2、hs-CRP及ABI的多元线性回归分析

Table 3 Multiple linear regression analysis on correlations of SDNN with Lp-PLA2, hs-CRP and ABI in patients with CHD

变量	B	SE	β	t值	P值
常量	83.202	12.347	—	6.739	<0.01
Lp-PLA2	-0.040	0.014	-0.122	-2.924	0.004
hs-CRP	-4.388	1.215	-0.151	-3.611	<0.01
ABI	43.301	10.537	0.159	4.109	<0.01

注: “—”为无此项数据

2.4 预测价值 ROC曲线显示, Lp-PLA2预测CHD患者ABI异常的曲线下面积(AUC)为0.583[95%CI(0.480, 0.687)], 灵敏度为0.84、特异度为0.38, 见图7。Lp-PLA2预测CHD患者SDNN异常的AUC为0.656[95%CI(0.600, 0.712)], 灵敏度为0.76, 特异度为0.48, 见图8。



注: hs-CRP= 超敏 C 反应蛋白

图6 SDNN 与 CHD 患者 hs-CRP 相关性的散点图

Figure 6 Scatter plot for correlation between SDNN and hs-CRP in patients with CHD

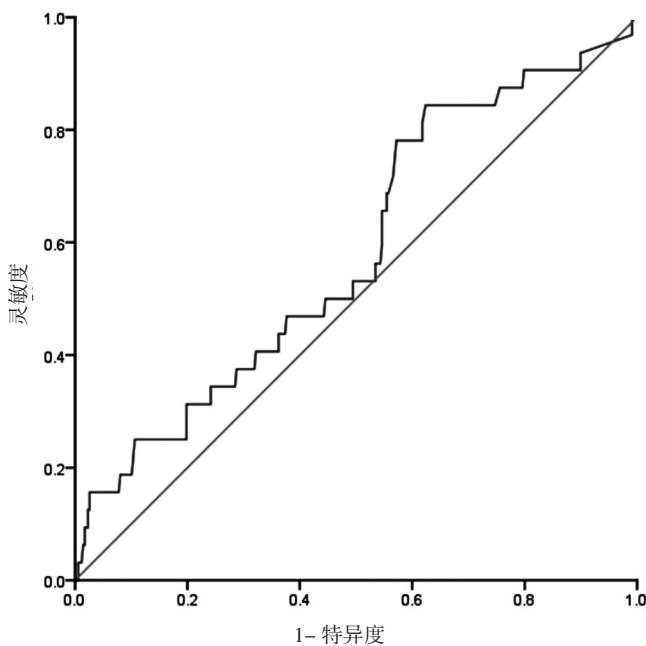


图7 Lp-PLA2 对 CHD 患者 ABI 异常预测值的 ROC 曲线

Figure 7 ROC curve for Lp-PLA2 in predicting ABI abnormality in patients with CHD

3 讨论

研究表明,慢性炎症反应在冠状动脉粥样硬化进展过程中扮演着重要角色^[11],因此相关研究人员试图采用一系列炎症标志物来预测冠状动脉病变的发生发展。大量临床研究证实,Lp-PLA2 是诊断 CHD 的新型炎症标志物^[12-14],且其与冠状动脉狭窄程度呈正相关^[15],可预测冠状动脉狭窄程度^[16]。Lp-PLA2 主要由动脉粥样硬化斑块中的巨噬细胞分泌,可促使巨噬细胞转变成泡沫细胞^[14],导致斑块不稳定,诱发心绞痛甚至急性冠脉综合

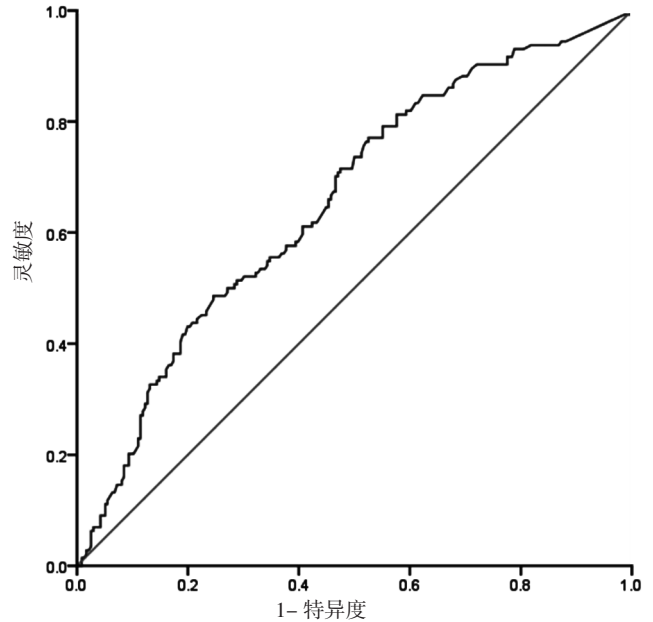


图8 Lp-PLA2 对 CHD 患者 SDNN 异常预测值的 ROC 曲线

Figure 8 ROC curve for Lp-PLA2 in predicting SDNN abnormality in patients with CHD

征。ABI 可用于下肢外周动脉疾病的筛查^[1, 17]及预测冠状动脉狭窄^[2]。HRV 降低与 CHD 患者心力衰竭^[18]、恶性心律失常^[19]及冠状动脉狭窄程度^[20-21]呈正相关。因此理论上 Lp-PLA2 与 CHD 患者 ABI、HRV 相关。

CHD 的常见危险因素主要包括年龄、Hcy、糖代谢异常、脂代谢异常(包括 TC、LDL-C 升高, ApoA、HDL-C 降低等)、炎症反应等,且 CHD 患者易出现 ABI 及 HRV 降低。本研究结果显示,B 组患者年龄、Hcy、HbA_{1c}、Lp(a)、hs-CRP、Lp-PLA2 高于 A 组, ApoA、HDL-C、ABI、SDNN 及 TC、LDL-C 等低于 A 组,笔者推测这可能与确诊的患者多在口服他汀类药物有关。

本研究结果显示,Lp-PLA2 与 CHD 患者 SDNN 呈负相关,并对 CHD 患者 SDNN 异常有一定预测价值,分析其机制可能为:冠状动脉粥样硬化斑块越多,巨噬细胞分泌的 Lp-PLA2 越多,冠状动脉狭窄越严重,易引发心肌缺血缺氧,导致心脏自主神经功能失常,进而造成 HRV 降低。多项研究表明,Lp-PLA2 与冠状动脉狭窄相关^[7-9],而冠状动脉狭窄与 ABI 相关^[2],因此理论上 Lp-PLA2 与 CHD 患者 ABI 应有一定关系,但本研究结果显示,Lp-PLA2 与 CHD 患者 ABI 无关,可能原因如下:(1) Lp-PLA2 是炎症指标,其在稳定型心绞痛及急性冠脉综合征患者中的分泌水平不一,而本研究对象未细分为稳定型心绞痛和急性冠脉综合征;(2) 本研究样本量较小;(3) Lp-PLA2 具有血管特异性,

在不同血管内环境下的分泌机制不同; (4) Lp-PLA2 由不同细胞分泌^[22]。

综上所述, CHD 患者 Lp-PLA2 升高, ABI、HRV 降低; Lp-PLA2 与 CHD 患者 HRV 呈负相关且对 HRV 异常有一定预测价值, 但其与 CHD 患者 ABI 无关, 而 ABI 与 CHD 患者 HRV 呈正相关; 今后需将 CHD 患者细分为稳定型心绞痛与急性冠脉综合征, 扩大样本量并通过建立动物模型验证 Lp-PLA2 的血管或细胞特异性, 进而验证 Lp-PLA2 与 ABI 的关系。

作者贡献: 刘向阳、唐良秋进行文章的构思与设计; 刘向阳、李爱华进行数据收集、整理、分析; 刘向阳进行结果分析与解释, 撰写论文; 唐良秋负责文章的质量控制及审校, 对文章整体负责, 监督管理。

本文无利益冲突。

参考文献

- [1] KEVEN A, DURMAZ M S. The importance of community screening of asymptomatic elderly for peripheral arterial disease by Doppler ultrasound and ankle-brachial index [J]. *J Ultrason*, 2017, 17(71): 235-240. DOI: 10.15557/JoU.2017.0034.
- [2] DE OLIVEIRA D C, CORREIA A, NASCIMENTO NETO J, et al. Association Between Ankle-Brachial Index and Coronary Lesions Assessed by Coronary Angiography [J]. *Cardiol Res*, 2015, 6(1): 216-220. DOI: 10.14740/cr376w.
- [3] KUBOTA Y, CHEN L Y, WHITSEL E A, et al. Heart rate variability and lifetime risk of cardiovascular disease: the Atherosclerosis Risk in Communities Study [J]. *Ann Epidemiol*, 2017, 27(10): 619-625. DOI: 10.1016/j.annepidem.2017.08.024.
- [4] PIZZI C, MANZOLI L, MANCINI S, et al. Analysis of potential predictors of depression among coronary heart disease risk factors including heart rate variability, markers of inflammation, and endothelial function [J]. *Eur Heart J*, 2008, 29(9): 1110-1117. DOI: 10.1093/eurheartj/ehn137.
- [5] 刘向阳, 唐良秋, 范文茂, 等. 脂蛋白相关磷脂酶 A2 对冠心病患者反杓型血压及冠状动脉重度狭窄的诊断价值分析 [J]. *实用心脑血管病杂志*, 2019, 27(7): 88-92. DOI: 10.3969/j.issn.1008-5971.2019.07.018.
LIU X Y, TANG L Q, FAN W M, et al. Diagnostic value of Lp-PLA2 on reverse-dipper blood pressure and severe stenosis of coronary artery in patients with coronary heart disease [J]. *Practical Journal of Cardiac Cerebral Pneumal and Vascular Disease*, 2019, 27(7): 88-92. DOI: 10.3969/j.issn.1008-5971.2019.07.018.
- [6] GARG P K, MCCLELLAND R L, JENNY N S, et al. Lipoprotein-associated phospholipase A2 and risk of incident cardiovascular disease in a multi-ethnic cohort: The multi ethnic study of atherosclerosis [J]. *Atherosclerosis*, 2015, 241(1): 176-182. DOI: 10.1016/j.atherosclerosis.2015.05.006.
- [7] WALLENTIN L, HELD C, ARMSTRONG P W, et al. Lipoprotein-Associated Phospholipase A2 Activity Is a Marker of Risk But Not a Useful Target for Treatment in Patients With Stable Coronary Heart Disease [J]. *J Am Heart Assoc*, 2016, 5(6): 1-16. DOI: 10.1161/JAHA.116.003407.
- [8] BENDERLY M, SAPIR B, KALTER-LEIBOVICI O, et al. Lipoprotein-associated phospholipase A2, and subsequent cardiovascular events and mortality among patients with coronary heart disease [J]. *Biomarkers*, 2017, 22(3/4): 219-224. DOI: 10.3109/1354750X.2016.1171910.
- [9] 郭攸胜, 周文娟, 骆骅, 等. ABI、baPWV 及血浆 Lp-PLA2 水平与冠心病关系的研究 [J]. *心血管康复医学杂志*, 2015, 24(5): 508-512. DOI: 10.3969/j.issn.1008-0074.2015.05.11.
GUO Y S, ZHOU W J, LUO H, et al. Relationship among ABI, baPWV, plasma Lp-PLA2 level and coronary heart disease [J]. *Chinese Journal of Cardiovascular Rehabilitation Medicine*, 2015, 24(5): 508-512. DOI: 10.3969/j.issn.1008-0074.2015.05.11.
- [10] 张伟伟. 长程心率变异性与血 Lp-PLA2 的含量及冠脉病变关系的研究 [D]. 哈尔滨: 哈尔滨医科大学, 2012.
- [11] 中华心血管病杂志编委会心率变异性对策专题组. 心率变异性检测临床应用的建议 [J]. *中华心血管病杂志*, 1998, 26(4): 12-15. DOI: 10.3760/j.issn: 0253-3758.1998.04.003.
- [12] LIBBY P. Inflammation in atherosclerosis [J]. *Nature*, 2002, 420(6917): 868-874. DOI: 10.1038/nature01323.
- [13] IKONOMIDIS I, KADOGLU N N, TRITAKIS V, et al. Association of Lp-PLA2 with digital reactive hyperemia, coronary flow reserve, carotid atherosclerosis and arterial stiffness in coronary artery disease [J]. *Atherosclerosis*, 2014, 234(1): 34-41. DOI: 10.1016/j.atherosclerosis.2014.02.004.
- [14] GILSTRAP L G, WANG T J. Biomarkers and cardiovascular risk assessment for primary prevention: An update [J]. *Clin Chem*, 2012, 58(1): 72-82. DOI: 10.1373/clinchem.2011.165712.
- [15] 刘向阳, 唐良秋, 范文茂, 等. 不同血压昼夜节律冠心病患者血浆同型半胱氨酸、血清脂蛋白相关磷脂酶 A2 水平变化及其与冠状动脉狭窄程度的关系研究 [J]. *实用心脑血管病杂志*, 2019, 27(1): 30-35. DOI: 10.3969/j.issn.1008-5971.2019.01.007.
LIU X Y, TANG L Q, FAN W M, et al. Changes of plasma Hcy level, serum LP-PLA2 level in coronary heart disease patients with different circadian rhythm of blood pressure and their relations with severity of coronary stenosis [J]. *Practical Journal of Cardiac Cerebral Pneumal and Vascular Disease*, 2019, 27(1): 30-35. DOI: 10.3969/j.issn.1008-5971.2019.01.007.
- [16] 刘季晨, 郭凯, 卢浩, 等. 红细胞分布宽度联合脂蛋白相关磷脂酶 A2 检测可提高冠心病患者的冠状动脉狭窄程度诊断的准确性 [J]. *南方医科大学学报*, 2016, 36(6): 875-879. DOI: 10.3969/j.issn.1673-4254.2016.06.25.
LIU J C, GUO K, LU H, et al. Red blood cell distribution width combined with lipoprotein-associated phospholipase A2 detection for improving diagnostic accuracy of coronary artery stenosis in patients with coronary artery disease [J]. *Journal of Southern Medical University*, 2016, 36(6): 875-879. DOI: 10.3969/

- j.issn.1673-4254.2016.06.25.
- [17] 郑黎强, 余金明, 李觉, 等. 冠心病及等危症住院患者踝臂指数及下肢外周动脉疾病患病率调查 [J]. 中国动脉硬化杂志, 2007, 15 (11): 857-860. DOI: 10.3969/j.issn.1673-4254.2016.06.25.
- ZHENG L Q, YU J M, LI J, et al. Mean Level of Ankle-Brachial Index and Prevalence of Peripheral Arterial Disease Among Inpatients with Equal-Risk to Coronary Heart Disease [J]. Chinese Journal of Arteriosclerosis, 2007, 15 (11): 857-860. DOI: 10.3969/j.issn.1673-4254.2016.06.25.
- [18] PATEL V N, PIERCE B R, BODAPATI R K, et al. Association of Holter-Derived Heart Rate Variability Parameters With the Development of Congestive Heart Failure in the Cardiovascular Health Study [J]. JACC Heart Fail, 2017, 5 (6): 423-431. DOI: 10.1016/j.jchf.2016.12.015.
- [19] 杨法, 苏明兰, 李小珠, 等. T波电交替、心率变异联合检测对急性心肌梗死患者恶性心律失常预测评估的作用 [J]. 白求恩医学杂志, 2016, 14 (3): 272-274. DOI: 10.16485/j.issn.2095-7858.2016.03.003.
- YANG F, SU M L, LI X Z, et al. The value of TWA and HRV in predicting malignant arrhythmia in AMI patients [J]. Journal of Bethune Military Medical College, 2016, 14 (3): 272-274. DOI: 10.16485/j.issn.2095-7858.2016.03.003.
- [20] 周琪, 梁有峰, 丁汝跃, 等. 冠心病患者心率变异性及血浆同型半胱氨酸水平与冠脉病变程度有相关性 [J]. 心脏杂志, 2016, 28 (3): 299-301, 308. DOI: 10.13191/j.chj.2016.0080.
- ZHOU Q, LIANG Y F, DING R Y, et al. Correlation of plasma homocysteine and heart rate variability with severity of coronary artery heart disease [J]. Chinese Heart Journal, 2016, 28 (3): 299-301, 308. DOI: 10.13191/j.chj.2016.0080.
- [21] 邹小兰, 王建榜. 心率变异性与冠心病冠脉病变程度的相关性分析 [J]. 心血管康复医学杂志, 2018, 27 (3): 268-271. DOI: 10.3969/j.issn.1008-0074.2018.03.08.
- ZOU X L, WANG J B. Correlation between heart rate variability and severity of coronary artery lesion in patients with coronary heart disease [J]. Chinese Journal of Cardiovascular Rehabilitation Medicine, 2018, 27 (3): 268-271. DOI: 10.3969/j.issn.1008-0074.2018.03.08.
- [22] ZHENG G H, XIONG S Q, MEI L J, et al. Elevated plasma platelet activating factor, platelet activating factor acetylhydrolase levels and risk of coronary heart disease or blood stasis syndrome of coronary heart disease in Chinese: A case control study [J]. Inflammation, 2012, 35 (4): 1419-1428. DOI: 10.1007/s10753-012-9455-4.
- (收稿日期: 2019-11-11; 修回日期: 2020-02-28)
(本文编辑: 刘新蒙)
-
- (上接第 43 页)
- [9] 中华医学会心血管病学分会, 中华心血管病杂志编辑委员会. 中国心力衰竭诊断和治疗指南 2014 [J]. 中华心血管病杂志, 2014, 42 (2): 98-122. DOI: 10.3760/cma.j.issn.0253-3758.2014.02.004.
- [10] 马建斌, 王赞, 王东, 等. 心血管急症伴发晕厥患者发生死亡风险的临床研究 [J]. 中华急诊医学杂志, 2018, 27 (5): 541-547. DOI: 10.3760/cma.j.issn.1671-0282.2018.05.016.
- MA J B, WANG Y, WANG D, et al. Clinical study of correlation between syncope and risk of death in patients with cardiovascular emergencies [J]. Chinese Journal of Emergency Medicine, 2018, 27 (5): 541-547. DOI: 10.3760/cma.j.issn.1671-0282.2018.05.016.
- [11] 李明亮, 陈强. 血清总 T3 和游离 T4 水平与急性心肌梗死后心力衰竭发生的相关性研究 [J]. 临床心血管病杂志, 2018, 34 (4): 338-342. DOI: 10.13201/j.issn.1001-1439.2018.04.007.
- LI M L, CHEN Q. Correlation between serum total T3 and free T4 levels and heart failure after acute myocardial infarction [J]. Journal of Clinical Cardiology, 2018, 34 (4): 338-342. DOI: 10.13201/j.issn.1001-1439.2018.04.007.
- [12] 郭刚, 吴先正, 苏立杰. 急诊 BNP 和乳酸检测对急性心肌梗死病人病情及预后评估的价值 [J]. 中西医结合心脑血管病杂志, 2017, 15 (1): 76-79. DOI: 10.3969/j.issn.1672-1349.2017.01.022.
- [13] CHO J, PARK I B, LEE K, et al. Statin has more protective effects in AMI patients with higher plasma BNP or NT-proBNP level, but not with lower left ventricular ejection fraction [J]. J Cardiol, 2018, 71 (4): 375-381. DOI: 10.1016/j.jcc.2017.10.009.
- [14] ASADI N, KHERADMAND A, GHOLAMI M, et al. Effect of ghrelin on the biochemical and histopathology parameters and spermatogenesis cycle following experimental varicocele in rat [J]. Andrologia, 2018, 50 (10): e13106. DOI: 10.1111/and.13106.
- [15] 田双全, 富路. Ghrelin 抗心力衰竭机制研究进展 [J]. 医学综述, 2018, 24 (10): 2022-2026. DOI: 10.3969/j.issn.1006-2084.2018.10.030.
- TIAN S Q, FU L. Research Progress of Anti-Heart Failure Mechanism of Ghrelin [J]. Medical Recapitulate, 2018, 24 (10): 2022-2026. DOI: 10.3969/j.issn.1006-2084.2018.10.030.
- [16] LUND L H, WILLIAMS J J, FREDA P, et al. Ghrelin resistance occurs in severe heart failure and resolves after heart transplantation [J]. Eur J Heart Fail, 2009, 11 (8): 789-794. DOI: 10.1093/eurjhf/hfp088.
- (收稿日期: 2019-11-20; 修回日期: 2020-02-20)
(本文编辑: 李越娜)