血浆 IIA 分泌型磷脂酶 A2 水平与冠脉支架术后再狭窄关系

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摘要 目的:测定稳定型冠心病患者支架植入术(percutanous coronary intervention ,PCI)前血浆 IIA 分泌型磷脂酶 A2(group IIA secretory phospholipase A2,Ⅱ A-sPLA2)的水平,以探讨该酶与冠脉支架术后再狭窄的可能关系。方法:稳定型冠心病行 PCI 患者 63 例,非冠心病患者 39 例,健康正常对照组 42 例,分别取外周静脉血测定血浆Ⅱ A-sPLA2 酶浓度。PCI 患者 6 个月后复查造影。结果:PCI 患者术前该酶浓度显著高于正常对照组(P<0.05),支架内再狭窄率 34.9 %,再狭窄(restenosis,RS)患者支架术前该酶水平与无再狭窄患者该酶水平无统计学差异(P>0.05)。结论:PCI 患者术前血浆Ⅱ A-sPLA2 酶浓度显著高于正常对照组,但可能与支架术后再狭窄无关。

关键词:Ⅱ A 分泌型磷脂酶 A2;高敏 C- 反应蛋白;支架植入术;再狭窄

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Relationship Between Plasma IIA Secretory Phospholipase A2 and Restenosis after Percutanous Coronary Intervention in Patients with Coronary Heart Disease

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ABSTRACT Objective: To study the correlation between IIA-sPLA2 level and restenosis after percutanous coronary intervention (PCI) in Patients with coronary heart disease. Methods: This study enrolled 63 patients with coronary heart disease (CHD) who underwent successful PCI,39 patients with non-CHD, and 42 healthy subjects were studied as a control group .Levels of IIA-sPLA2 in plasma were measured by an enzymoimmunoassay using a monoclonal antibody. The patients who underwent PCI had repeat angiography at six-month follow-up. Results: The level of IIA-sPLA2 in PCI patients was significantly higher than that in healthy subjects (P<0.05), but not higher than that in patients with non-CHD (P>0.05). Restenosis occurred in 22 patients (34.9 %). While there were no significantly changes of the levels of IIA-sPLA2 between the patients without or with restenosis. Conclusions: The level of IIA-sPLA2 in patients with coronary heart disease had a significant increase compared to the healthy subjects, but such increase may not be associated with in-stent restenosis.

Key words: Group IIA secretory phospholipase A2; High sensitive C-reactive protein; Percutanous coronary intervention; Restenosis

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前言

冠心病患者支架植入术成为临床上治疗冠心病的重要手段之一,但是术后再狭窄严重影响其远期疗效[1],炎症可能参与了再狭窄的全过程[2]。血浆Ⅱ A 分泌型磷脂酶 A2 作为一个炎症因子,在动脉粥样硬化发生发展过程中可能起了重要角色[3],本文探讨冠心病患者 PCI 术前该酶浓度与再狭窄的可能关系。

1 资料和方法

1.1 临床资料

2009 年 2 月至 2010 年 2 月在我院心内科住院,并接受普通支架植入术的稳定型冠心病患者 63 例 (PCI 组),男性 43 例,女性 20 例,平均年龄(65.37± 9.76)岁。入选标准:①有临床心绞痛症状②冠状动脉主要血管(即左主干、前降支、回旋支、右冠状动脉)罪犯血管(target vascular)管腔狭窄程度≥ 75 %。排除标准:急性冠脉综合症、近期外科手术或创伤、此前 1 个月内患有严重的感染性疾病、恶性肿瘤、慢性炎症性疾病(包括类风湿性关节炎、骨关节炎、肠炎等)、慢性结缔组织病等。非冠心病组:同期因胸痛或 ECG 显示有局部缺血改变,经冠脉造影显示为正常冠脉或狭窄 <50%,共 39 例,男性 18 例,女性 21 例,年龄(62.03± 9.27)岁;正常对照组 42 例选自我院健康体检者,男性 17 例,女性 25 例,年龄(64.17± 10.83)岁。所有 PCI 患者 6 个月后复查冠脉造影,再狭窄标准[4]:冠脉造影显示支架内管腔狭窄超过内径的 50 %。正常对照组及实验组基本情况见表 1。

1.2 方法

Ⅱ A-sPLA2:人Ⅱ A-sPLA2 定量检测(ELISA)试剂盒,R&D 公司产品,BIO-RAD Model 680 型酶标仪测定。总胆固醇(TC)、甘油三酯(TG)为北京中生北控公司产品,采用酶法;高

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密度脂蛋白胆固醇（HDL-C）、低密度脂蛋白胆固醇（LDL-C）为日本第一化学公司产品，采用酶法；血糖（Glu）为上海德赛公司产品，己糖激酶法；肌酐（Cre）为四川迈克科技股份有限公司产品，酶法测定；高敏 C 反应蛋白（high sensitive C-Reactive Protein, hs- CRP）为芬兰 ORION 公司产品，采用胶乳增强免疫比浊法，以上指标均由 Olympus AU5400 全自动生化分析仪测定。

表 1 正常对照组及实验组基本情况（$\bar{x}\pm s$）

Table 1 Baseline characteristics of control and study groups

Item	Control group (n=42)	Non-CHD group (n=39)	CHD with PCI group (n=63)
Male (%)	17 (40.5 %)	18 (46.2 %)	43 (68.3 %)
Age (yrs)	64.17± 10.83	62.03± 9.27	65.37± 9.76
Glu (mmol/L)	5.33± 0.76	6.37± 1.69*	7.55± 3.94*
Cre (μmmol/L)	67.28± 19.05	86.69± 26.43*	93.56± 25.68*
TC (mmol/L)	4.80± 0.72	4.28± 0.74*	4.35± 1.04*
TG (mmol/L)	1.05± 0.35	1.23± 0.61	1.54± 1.06*
HDL-C (mmol/L)	1.42± 0.20	1.12± 0.32*	1.00± 0.27*
LDL-C (mmol/L)	2.42± 0.83	2.61± 0.74	2.84± 1.00

注：* 与正常对照组比较，P<0.05

Note: *P<0.05 Compared with Control group

1.3 统计学处理

使用 SPSS 11.0 软件进行统计分析，偏态分布资料以中位数（四分位数间距）表示，正态分布资料以均数± 标准差（$\bar{x}\pm s$）表示，均数比较采用 F 检验及 t 检验；ⅡA-sPLA2 与 hs-CRP 之间关系采用等级相关检验；通过受试者工作曲线（ROC 曲线）判断其诊断价值。以 P<0.05 为有统计学差异。

2 结果

2.1 三组血浆ⅡA-sPLA2 浓度和 hs-CRP 浓度比较

血浆ⅡA-sPLA2 浓度和 hs-CRP 浓度比较见表 2。非冠心病组及冠心病 PCI 组血浆ⅡA-sPLA2 浓度均显著高于正常对照组（P<0.05），而冠心病 PCI 组与非冠心病组间无统计学差异（P>0.05）。冠心病 PCI 组 hs-CRP 浓度显著高于正常对照组（P<0.05），非冠心病组 hs-CRP 浓度与正常对照组及冠心病 PCI 组间均无统计学意义（P>0.05）。

表 2 血浆ⅡA-sPLA2 浓度和 hs-CRP 浓度比较

Table 2 Levels of ⅡA-sPLA2 and hs-CRP compared with each other

Item	Control group (n=42)	Non-CHD group (n=39)	CHD with PCI group (n=63)
ⅡA-sPLA2 (pg/mL)	178(138,218)	334(183,442)*	345(231,399)*
Hs-CRP (mg/L)	1.88± 2.47	2.25± 3.88	3.87± 4.86*

注：* 与正常对照组比较，P<0.05

Note: *P<0.05 Compared with Control group

2.2 正常对照组、非冠心病组、PCI 再狭窄组及 PCI 无再狭窄组血浆ⅡA-sPLA2 浓度及血清 hs-CRP 浓度比较

所有 PCI 患者 6 个月后复查冠脉造影，共有 22 例发生再狭窄，再狭窄率 34.9 %。四组间血浆ⅡA-sPLA2 浓度及血清 hs-CRP 浓度比较见图 1、图 2。

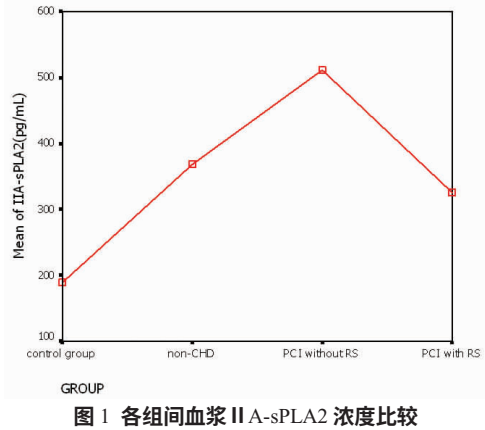

图 1 各组间血浆ⅡA-sPLA2 浓度比较

Fig.1 The comparison on levels of ⅡA-sPLA2 in plasma for each group

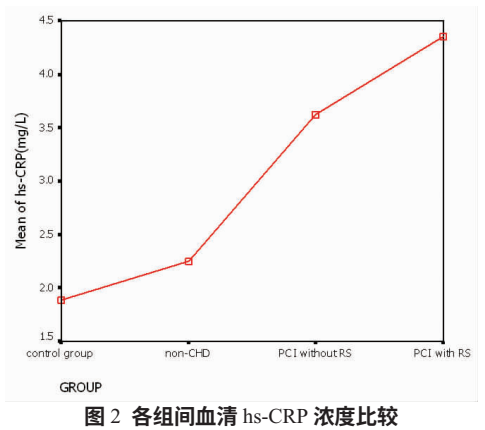

图 2 各组间血清 hs-CRP 浓度比较

Fig.2 The comparison on levels of hs-CRP in serum for each group

2.3 ⅡA-sPLA2 及 hs-CRP 的 ROC 曲线

ⅡA-sPLA2 及 hs-CRP 对冠心病的诊断价值（ROC 曲线）见图 3。

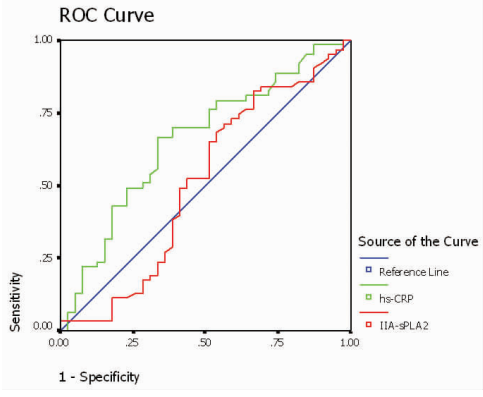

图 3 ⅡA-sPLA2 及 hs-CRP 的 ROC 曲线

Fig.3 The ROC Curves of ⅡA-sPLA2 and hs-CRP

3 讨论

ⅡA-sPLA2 作为磷脂酶 A2 家族成员，它能水解细胞膜和脂蛋白磷脂 2 位（Sn2）脂键[5]，从而产生游离脂肪酸和溶血卵磷脂，水解产物又可以被进一步代谢为广泛参与细胞内各种炎性变化的介质[6]。冠心病的炎症发病机制在临床正广泛受到关注，国内外研究显示，心血管疾病患者ⅡA-sPLA2 血浆浓度是增高的，高浓度的ⅡA-sPLA2 是一个独立危险因子和重要的预测因子[7-11]。本文也显示冠心病 PCI 组及非冠心病组血浆ⅡA-sPLA2 浓度均显著高于健康对照组，但是冠心病 PCI 组酶浓度虽高于非冠心病组，但是两组之间并无统计学差异，也就是说ⅡA-sPLA2 在区分有冠心病及无冠心病方面价值甚小，从 ROC 曲线下面积也可看出，其对于冠心病的诊断价值低于 hs-CRP（曲线下面积分别为 0.509 与 0.657）。

血管内再狭窄已经成为影响血管修复术长期疗效的一个重要限制因素，冠脉支架的广泛应用也导致了一个更加剧烈和长期的炎症状态[12]。sPLA2 不仅是一个炎症标志物，而且它可能直接参与了再狭窄的进展[13]。国外研究[14-16]也阐明了ⅡA-sPLA2 与 RS 的可能关系，但是本文 PCI 再狭窄组ⅡA-sPLA2 浓度并不高于无再狭窄组，可能与本研究病例数太少，研究对象产生偏倚所致。同时对ⅡA-sPLA2 及 hs-CRP 进行 Spearman 等级相关检验，发现二者间并无相关性。

总之，冠心病是一个多因素复杂疾病，支架术后再狭窄机制复杂[17]，现今关于炎症因子与再狭窄关系研究较多，炎症因子在再狭窄中的预测价值还有赖于大样本、科学严谨的临床试验加以验证。

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导。同时,医院也可以主动组织医护人员及患者与厂商进行交流。

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