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lp-PLA2、RBP 与冠心病病变程度相关性及其疾病诱发的危险因素分析*

王正芳 姜润涵 吴天学 徐 薇 刁叶秋[△]

(扬州大学附属苏北人民医院医学检验科 江苏 扬州 225001)

摘要 目的:研究脂蛋白磷脂酶 A2(lp-PLA2)、视黄醇结合蛋白(RBP)与冠心病(CAD)病变程度的相关性及其疾病诱发的危险因素。**方法:**以 2019 年 12 月至 2021 年 12 月在本院诊治的冠心病患者 140 例作为研究对象,所有患者均进行冠状动脉造影检查,并根据冠状动脉侧支循环形成情况进行分级。所有患者都给予血清 lp-PLA2、RBP 检测并进行相关性、危险因素分析。**结果:**在 140 例患者中,冠状动脉侧支循环未形成 40 例(对照组),冠状动脉侧支循环形成 100 例(研究组),研究组中 I 级 40 例,II 级 38 例,III 级 22 例。研究组的血清 lp-PLA2、RBP 含量都高于对照组($P<0.05$);不同分级患者的血清 lp-PLA2、RBP 含量对比也有明显差异($P<0.05$)。在冠心病患者中,Spearsman 相关分析显示血清 lp-PLA2、RBP 含量与侧支循环形成分级存在正相关性($P<0.05$)。logistic 回归分析显示血清 lp-PLA2、RBP 含量均为影响冠心病患者侧支循环形成分级的危险因素($P<0.05$)。ROC 曲线分析显示血清 lp-PLA2、RBP 含量预测冠心病患者侧支循环分级的曲线下面积为 0.891、0.805。**结论:**随着冠状动脉侧支循环形成,冠心病患者的血清 lp-PLA2、RBP 含量明显增加,lp-PLA2、RBP 与侧支循环形成分级存在相关性,也是影响侧支循环分级的危险因素,也可预测侧支循环分级状况。

关键词:冠状动脉侧支循环形成;冠心病;脂蛋白磷脂酶 A2;视黄醇结合蛋白

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Correlation between lp-PLA2, RBP and The Degree of Coronary Heart Disease and The Risk Factors of Disease-induced Disease*

WANG Zheng-fang, JIANG Run-han, WU Tian-xue, XU Wei, DIAO Ye-qiu[△]

(Department of Medical Laboratory, North Jiangsu People's Hospital Affiliated to Yangzhou University, Yangzhou, Jiangsu, 225001, China)

ABSTRACT Objective: To explore and analysis the correlation between lipoprotein phospholipase A2 (lp-PLA2), retinol-binding protein (RBP) and the degree of coronary heart disease and the risk factors of disease-induced disease. **Methods:** 140 patients with coronary heart disease who were diagnosed and treated in our hospital from December 2019 to December 2021 were selected as the research subjects. All patients underwent coronary angiography and were graded according to the formation of coronary collateral circulation. All patients were given serum lp-PLA2, RBP detection and correlation and risk factor analysis. **Results:** Among the 140 patients, 40 patients had no coronary collateral circulation (matched group), 100 patients had coronary collateral circulation (research group), 40 patients had grade I, 38 had grade II, and 22 had grade III. The serum lp-PLA2 and RBP contents of the research group were higher than those of the matched group ($P<0.05$); the serum lp-PLA2 and RBP contents of patients with different grades were also different ($P<0.05$). In patients with coronary heart disease, Spearsman correlation analysis showed that serum lp-PLA2 and RBP levels were positive correlated with the grade of collateral circulation formation ($P<0.05$). Logistic regression analysis showed that serum lp-PLA2 and RBP levels were both risk factors for the formation of collateral circulation in patients with coronary heart disease ($P<0.05$). ROC curve analysis showed that the areas under the curve of serum lp-PLA2 and RBP levels for predicting collateral circulation grade in patients with coronary heart disease were 0.891 and 0.805. **Conclusion:** With the formation of coronary collateral circulation, the serum levels of lp-PLA2 and RBP in patients with coronary heart disease are significantly increased. Prediction of collateral circulation grading status.

Key words: Coronary collateral circulation; Coronary heart disease; Lipoprotein phospholipase A2; Retinol-binding protein

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前言

冠心病全称为冠状动脉粥样硬化性心脏病(Coronary

artery disease, CAD), 是一类主要由冠状动脉血管壁粥样硬化所引起的缺血性心脏病。随着经济社会发展、人口老龄化进程加快与人民生活水平提高, 冠心病正严重威胁着人民健康, 成

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作者简介:王正芳(1981-),女,本科,主管技师,研究方向:检验,电话:18051060318,E-mail:qyu85243@163.com

[△] 通讯作者:刁叶秋(1982-),女,本科,主管技师,研究方向:检验,电话:13912122818,E-mail:qyu85243@163.com

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为目前重要的公共卫生问题^[12]。冠心病的具体发病机制还不明确,主要由环境因素、遗传因素共同影响所致^[3]。当前对于冠心病病变程度的判断指标还比较少,在临床上多采用超声进行判定,但是存在一定的主观性,且判断的准确性有待提高。冠脉造影为诊断冠心病的金标准,还可判断患者的侧支循环状况^[4,5]。侧支循环是冠状动脉循环的储备力量,可以在冠脉病变提供代偿血供,也是正常心机的潜在供血通道^[6]。正常情况下侧支血管内没有血液流动,不过当机体发生冠心病时,可导致冠状动脉侧支循环的建立,形成代偿,为此判定侧支循环状况可有效判定患者的病情状况^[7,8]。不过冠脉造影毕竟为有创性检查,很难在临床上进行普查筛查。脂蛋白磷脂酶 A2 (Lipoprotein phospholipase A2, lp-PLA2)是钙依赖的磷脂酶家族成员,其高表达能促进释放大量炎症因子,也能够水解脂蛋白磷脂,从而对细胞膜运输产生影响,为此可参与多种心血管疾病的发生与发展^[9,10]。视黄醇结合蛋白(Retinol-binding protein, RBP)为主要反映机体炎症状况的指标,也具有控制血管新生的作用,可调节心血管疾病的发生^[11]。lp-PLA2 与 RBP 都可反映冠心病患者的病情状况,但是对冠状动脉侧支循环形成的判断尚无相关研究。基于此,本文具体探讨与分析了 lp-PLA2、RBP 与冠心病病变程度相关性及相关因素,现报道如下。

1 资料与方法

1.1 资料来源

选择 2019 年 12 月至 2021 年 12 月在本院诊治的冠心病患者 140 例作为研究对象。

纳入标准:符合冠心病的诊断标准(冠状动脉造影确诊);患者入院前 3 个月未服用影响血清 lp-PLA2、RBP 表达水平的药物;冠状动脉狭窄程度 20 %-70 %;研究得到医院伦理委员会的批准;患者病情稳定,非急诊患者,知情同意本研究。

排除标准:合并传染性疾病者;妊娠与哺乳期妇女;合并肿瘤

患者;合并严重心功能不全或肾功能不全者;合并脑梗塞、脑出血者患者;依从性不佳的患者。

1.2 冠状动脉侧支循环形成检查

所有患者都给予冠状动脉造影,采用猪尾巴导管行左心室造影,分为四级评定。冠状动脉侧支循环形成分级标准, I 级、II 级、III 级都可判断为冠状动脉侧支循环形成。0 级:冠状动脉造影无侧支循环显示; I 级:冠状动脉造影存在阻塞病变血管的细小分支显影,表现循环形成轻度丰富; II 级:冠状动脉造影存在阻塞病变血管主支远端缓慢显影,表现循环形成中度丰富; III 级:冠状动脉造影存在阻塞病变血管主支近端显影,表现循环形成重度丰富^[12]。

1.3 血清 lp-PLA2、RBP 检测

所有患者禁食 8 h 后,清晨空腹抽取静脉血 3 mL,于含分离胶的普通生化管(BD,美国)中;3500 rpm,离心 10 分钟后,分离血清,并置于 -40 ℃ 冰箱保存;室温复溶后对血清 lp-PLA2 (博源,苏州)、RBP 含量(科方,广州),进行测定,批内、批间的 CV 控制限都在 5.0 %以内。

1.4 统计方法

应用 SPSS21.00 软件对计量数据、计数数据进行分析, $P < 0.05$ 为差异具有统计学意义。以均数 $\pm$ 标准差、率等表示,对比为 t 检验与卡方分析,多组间对比为方差分析,相关性检验用 Spearman 相关分析,诊断价值分析采用 ROC 曲线分析,危险因素分析采用 logistic 回归分析,检验水准为 $\alpha = 0.05$ 。

2 结果

2.1 冠状动脉侧支循环形成情况

在 140 例患者中,冠状动脉侧支循环未形成 40 例(对照组),冠状动脉侧支循环形成 100 例(研究组),研究组中 I 级 40 例, II 级 38 例, III 级 22 例。研究组与对照组的一般资料对比无差异($P > 0.05$)。见表 1。

表 1 两组一般资料对比

Table 1 The comparison of the general data between the two groups

Groups	n	Gender (male / female)	Age (year)	Body mass index (kg/m ²)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)	Type of disease (acute myocardial infarction / unstable angina / stable angina)	Fasting blood glucose (mmol/L)
Research group	100	51/49	55.69 $\pm$ 2.32	22.48 $\pm$ 1.84	135.02 $\pm$ 10.34	84.32 $\pm$ 5.68	54/26/20	5.62 $\pm$ 0.24
Matched group	40	21/19	55.20 $\pm$ 3.11	22.09 $\pm$ 2.14	135.87 $\pm$ 11.33	84.44 $\pm$ 6.14	21/11/8	5.67 $\pm$ 0.24

2.2 血清 lp-PLA2、RBP 含量对比

研究组的血清 lp-PLA2、RBP 含量都高于对照组($P < 0.05$);不同分级患者的血清 lp-PLA2、RBP 含量对比也有明显差异($P < 0.05$)。见表 2。

2.3 相关性分析

在冠心病患者中, Spearman 相关分析显示血清 lp-PLA2、RBP 含量与侧支循环形成分级存在正相关性($P < 0.05$)。见表 3。

2.4 影响因素分析

在冠心病患者中,以侧支循环分级作为因变量,以血清 lp-PLA2、RBP 含量作为自变量, logistic 回归分析显示血清 lp-PLA2、RBP 含量都为影响冠心病患者侧支循环形成分级的危险因素($P < 0.05$)。见表 4。

2.5 预测价值分析

在冠心病患者中, ROC 曲线分析显示血清 lp-PLA2、RBP 含量预测冠心病患者侧支循环分级的曲线下面积为 0.891、0.805。具体见表 5、图 1。

表 2 两组血清 lp-PLA2、RBP 含量对比(pg/mL, 均数± 标准差)

Table 2 Comparison of serum lp-PLA2 and RBP content between the two groups (pg/mL, mean ± standard deviation)

Groups	n	lp-PLA2(U/L)	RBP(mg/L)
Research group	100	756.11± 33.95 [#]	86.29± 14.21 [#]
Matched group	40	443.01± 20.83	33.23± 8.11
Grade I	40	692.88± 25.24	75.14± 11.38
Grade II	38	755.48± 33.83 ^a	83.48± 13.81 ^a
Grade III	22	836.03± 52.25 ^{ab}	95.22± 17.39 ^{ab}

Note: compared with the matched group, [#]*P*<0.05, Comparison with grade I patients, ^a*P*<0.05, Comparison with grade II patients, ^b*P*<0.05.

表 3 血清 lp-PLA2、RBP 含量与冠心病病变程度相关性(n=140)

Table 3 Correlation between serum lp-PLA2 and RBP content and the degree of coronary heart disease lesions (n=140)

Index	lp-PLA2	RBP
r	0.733	0.672
P	0.000	0.000

表 4 影响冠心病患者侧支循环形成分级的危险因素(n=140)

Table 4 Risk factors affecting the grade of collateral circulation formation in CAD patients (n=140)

Index	β	SE	Wald	P	OR	95%CI
lp-PLA2	0.329	0.111	14.585	0.000	1.867	1.333-8.111
RBP	0.533	0.132	13.022	0.000	2.146	1.194-6.780

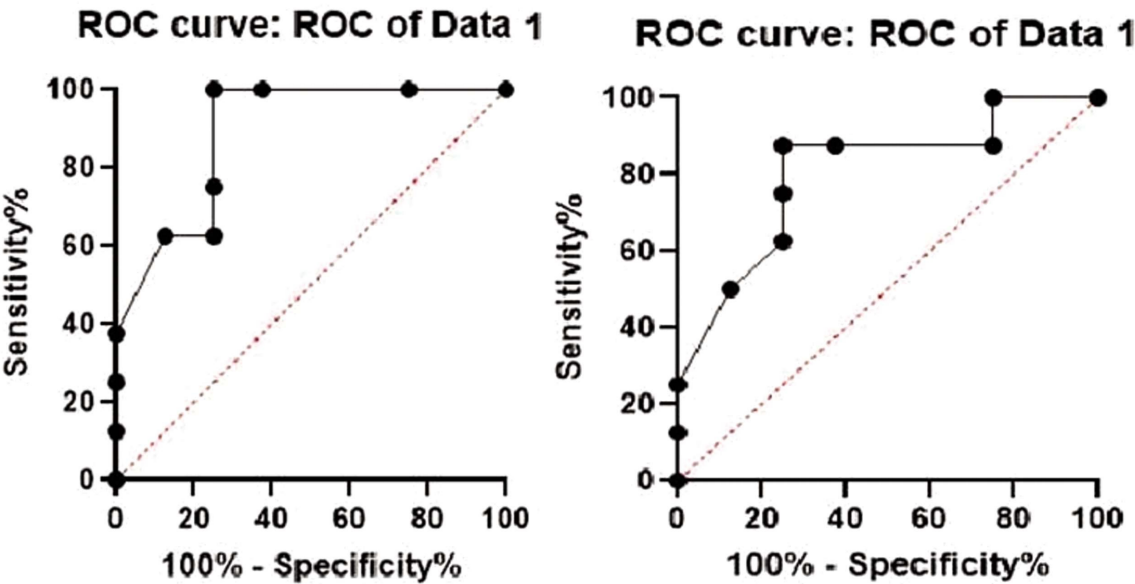


图 1 血清 lp-PLA2 含量、RBP 含量预测冠心病患者侧支循环分级的 ROC 曲线

Fig.1 The ROC curve of the serum lp-PLA2 content and the RBP content in predicting the collateral circulation grade in patients with coronary heart disease

表 5 血清 lp-PLA2、RBP 含量预测冠心病患者的 ROC 曲线分析(n=140)

Table 5 Analysis of the ROC curve of the predicted CAD patients with serum lp-PLA2 and RBP content (n=140)

Index	Area under curve	95%CI		Sensitivity	Specificity
		Upper limit	Lower limit		
lp-PLA2	0.891	0.764	0.913	81.0%	78.3%
RBP	0.805	0.713	0.830	78.9%	79.2%

3 讨论

当前世界范围内冠心病发病率呈上升趋势,是指冠状动脉粥样硬化使血管腔阻塞,导致心肌缺氧、缺血而引起的心脏病^[13,14]。冠心病的发病机制研究较复杂,在内外在各种因素的刺激下,血管内皮细胞被激活,致使T淋巴细胞、白细胞、单核细胞结合到血管内皮并迁移至内皮下,导致功能失调,使得低密度脂蛋白颗粒聚集到血管内皮下,转变成泡沫细胞,然后形成脂质条纹、纤维斑块,从而导致冠心病的发生^[15,16]。

本研究显示在140例患者中,冠状动脉侧支循环未形成40例(对照组),冠状动脉侧支循环形成100例(研究组),研究组中I级40例,II级38例,III级22例,也表明冠心病患者多伴有冠状动脉侧支循环形成。冠脉造影不仅能有效判定冠脉病变狭窄程度,还可准确测量血管和斑块大小和观察斑块的组成,也可明确冠状动脉有无侧支循环形成。冠心病患者如有较好的侧支循环形成,能有效防止狭窄程度增加,可为改善患者预后提供基础^[17]。

研究组的血清lp-PLA₂、RBP含量都高于对照组($P<0.05$);不同分级患者的血清lp-PLA₂、RBP含量对比也有明显差异($P<0.05$),表明冠心病患者多伴有血清lp-PLA₂、RBP含量的高表达,随着冠状动脉侧支循环形成,可促进血清lp-PLA₂、RBP的释放。该结果与吕留强等人^[18]的报道具有一致性。分析可知:冠状动脉侧支循环被认为是动脉粥样硬化早期防止管腔缩小的一种代偿机制,但是采用冠脉造影检查对患者有一定创伤,为此在临床上需要寻找合理的血清学检测指标^[19,20]。lp-PLA₂是一种参与调节和代谢的重要酶类,与胶原纤维一起位于巨噬细胞集聚区,催化产生多种脂质介质,可以引起脂质沉积。lp-PLA₂还可催化水解细胞膜和脂蛋白上的甘油磷脂形成溶血磷脂和非脂化脂肪酸,可介导泡沫细胞及粥样斑块的形成,进而介导产生易损斑块、动脉血栓^[21,22]。RBP是一种重要的转录因子,在调控心肌细胞迁移、动员、归巢等方面发挥重要作用,具有抑制血管新生的作用,也可加剧冠心病患者的病情;此外,其水平升高参与糖、脂代谢,可能间接诱导胰岛素抵抗,与代谢综合征密切相关,是动脉粥样硬化的危险因素,而动脉粥样硬化是冠心病的病理基础^[23,24]。

冠状动脉侧支循环形成是血管对血流阻力、动脉管壁损伤及血管内皮细胞增殖的代偿性反应,能在一定程度上保证病变血管有效血供,延迟患者的病情恶化^[25,26]。本研究Spearsman相关分析显示冠心病患者的血清lp-PLA₂、RBP含量与侧支循环形成分级存在正相关性;logistic回归分析显示血清lp-PLA₂、RBP含量都为影响冠心病患者侧支循环形成分级的危险因素;ROC曲线分析显示血清lp-PLA₂、RBP含量预测冠心病患者侧支循环分级的曲线下面积为0.891、0.805,表明lp-PLA₂、RBP与冠脉病变程度存在相关性,也是影响侧支循环分级的危险因素,也可预测侧支循环分级状况。该结果与张静^[27]等人的报道具有一致性。分析可知,lp-PLA₂、RBP的高表达可使血管内皮损伤,刺激血小板聚集,使得动脉粥样硬化风险也明显增加,从而使侧支循环形成重度丰富,引起冠心病的发生。lp-PLA₂还可以微粒体的形式释放入血,进入血管内皮细胞后,可参与血栓形成。RBP是体内一类将维生素从肝中转运至靶组织以及

实现维生素的细胞内转运代谢的特异性运载蛋白,在视黄醇被转至靶细胞之后,RBP释放入血可导致冠状动脉斑块处于不稳定状态。且其与脂质代谢密切相关,可通过增加糖原分解、限制糖原摄取、促进三酰甘油释放等导致糖脂代谢紊乱,引发肥胖、胰岛素抵抗以及冠心病等疾病的发生^[28-30]。因此,二者与冠心病冠心病患者侧支循环分级相关。本研究也存在一定的不足,未纳入健康人群进行对照分析,也没有判定其对侧支循环形成的预测作用,将在后续研究中探讨。

总之,随着冠状动脉侧支循环形成,冠心病患者的血清lp-PLA₂、RBP含量明显增加,lp-PLA₂、RBP与侧支循环形成分级存在相关性,也是影响侧支循环分级的危险因素,也可预测侧支循环分级状况。

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