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前列环素、神经肽 Y 与冠状动脉临界病变的关系及对近期功能性心肌缺血的预测研究 *

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摘要 目的:探讨与研究前列环素(PGI)、神经肽 Y(NPY)与冠状动脉临界病变的关系及对近期功能性心肌缺血的预测价值。**方法:**选择 2018 年 8 月到 2021 年 9 月本院诊治的 80 例冠状动脉临界病变患者与 80 例冠状动脉病患者分别作为临界组与病例组,同期选择在本院体检的正常冠状动脉人群 80 例作为正常组,检测三组前列环素、神经肽 Y 表达水平并进行相关性分析。随访冠状动脉临界病变患者的近期预后并进行功能性心肌缺血的预测分析。**结果:**病例组、临界组的血清前列环素含量低于正常组,血清神经肽 Y 含量高于正常组,病例组与临界组对比有明显差异($P<0.05$)。病例组、临界组的生理维度、社会维度、心理维度、环境维度等生命质量评分明显低于正常组,病例组也低于临界组($P<0.05$)。在 240 例人群中,Pearson 相关性分析显示血清前列环素、神经肽 Y 含量与冠状动脉临界病变的发生存在相关性($P<0.05$)。多因素 logistic 回归分析显示前列环素、神经肽 Y 为导致冠状动脉临界病变发生的重要因素($P<0.05$)。所有临界组患者预后随访到 2022 年 4 月,平均随访时间为 31.02 ± 2.58 个月,发生功能性心肌缺血 21 例,发生率为 26.3%。接收者操作特征(ROC)曲线分析显示血清前列环素、神经肽 Y 预测功能性心肌缺血的曲线下面积分别为 0.828、0.836。**结论:**冠状动脉临界病变患者多伴随有前列环素、神经肽 Y 表达异常,可导致生命质量下降,前列环素、神经肽 Y 与冠状动脉临界病变存在相关性,两者预测近期功能性心肌缺血的发生具有很好的价值。

关键词:前列环素;神经肽 Y;冠状动脉临界病变

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The Relationship between Prostacyclin, Neuropeptide Y and Critical Coronary Lesions and Prediction of Recent Functional Myocardial Ischemia*

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ABSTRACT Objective: To explore and study the relationship between Prostacyclin (PGI), neuropeptide Y (NPY) and critical coronary lesions and their predictive values for recent functional myocardial ischemia. **Methods:** From August 2018 to September 2021, 80 cases of patients with borderline coronary artery disease and 80 cases of patients with coronary artery disease who were diagnosed and treated in our hospital were selected as the borderline group and the case group, respectively, and the other 80 cases of patients with normal coronary artery who underwent physical examination in our hospital during the same period were selected as the normal group. The expression levels of prostacyclin and neuropeptide Y in the three groups were detected and the correlation analysis were carried out. To follow up the short-term prognosis of patients with borderline coronary artery disease and perform predictive analysis of functional myocardial ischemia. **Results:** The serum prostacyclin content of the case group and the borderline group were lower than that of the normal group, and the serum neuropeptide Y content were higher than that of the normal group ($P<0.05$). There were significant difference between the case group and the borderline group ($P<0.05$). The quality of life scores of the case group and the borderline group were significantly lower than those of the normal group, and the case group were also lower than the borderline group ($P<0.05$). In the 240 cases, Pearson correlation analysis showed that serum prostacyclin and neuropeptide Y levels were correlated with the occurrence of borderline coronary artery lesions ($P<0.05$). Multivariate logistic regression analysis showed that prostacyclin and neuropeptide Y were important factors leading to critical coronary lesions ($P<0.05$). All patients in the borderline group were followed up until April 2022, with an average follow-up time of 31.02 ± 2.58 months. There were 21 cases of functional myocardial ischemia occurred in the 80 cases, with an incidence rate of 26.3%. The receiver operating characteristic curve (ROC) curve analysis showed that the areas under the curve of serum prostacyclin and neuropeptide Y in predicting functional myocardial ischemia were 0.828 and 0.836, respectively. **Conclusion:** Patients with borderline coronary artery lesions are often accompanied by abnormal expressions of prostacyclin and neuropeptide Y, which can lead to decline in the quality of life. There are correlation between prostacyclin and neuropeptide Y and borderline coronary artery lesions, and they both have good values for predicting short-term functional myocardial ischemia.

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前言

冠状动脉临界病变当前在临床上比较常见,指冠状动脉造影显示冠状动脉的狭窄程度小于 50.0%,血管内超声的冠状动脉面积狭窄率在 40.0%-60.0%^[1]。冠状动脉临界病变是进展至冠状动脉病变的先决条件,也是导致急性冠状动脉综合征的罪犯血管,与近期功能性心肌缺血的发生与发展存在相关性^[2]。调查显示,每年因心血管病死亡的患者中,有一半是急性冠脉综合征所致,其中 20.0%由冠状动脉临界病变发生而来。加上冠状动脉临界病变征的突发性质,给医院医生及时救治和准确治疗带来了巨大挑战^[3,4]。冠状动脉临界病变的病理特点是动脉发生了非炎症性的退行性和增生性的病变,包括局部有脂质和复合糖类积聚,导致出血和血栓的形成^[5]。关于冠状动脉临界病变的发病机制有"脂质浸润学说"、"慢性炎症性学说"等,其中内皮细胞结构改变与功能失调是冠状动脉临界病变发病的重要机制,前列环素(Prostacyclin, PGI)是由血管内皮细胞合成,其在血清中水平的变化可反映机体血管内皮细胞的功能状态,从而可间接反映冠状动脉临界病变状况^[6,7]。神经肽 Y(Neuropeptide Y, NPY)广泛分布于外周交感神经、心脏和周围血管中,参与心血管功能活动的调节,主要由交感神经末

梢分泌,与冠状动脉病变及功能性心肌缺血的发生、发展密切相关^[8,9]。本文为此具体分析了前列环素、神经肽 Y 与冠状动脉临界病变的关系,并探讨了其对近期功能性心肌缺血的预测价值。现报道如下。

1 资料和方法

1.1 研究对象

选择 2018 年 8 月到 2021 年 9 月本院诊治的 80 例冠状动脉临界病变患者与 80 例冠状动脉病变患者分别作为临界组与病例组,同期选择在本院体检的正常冠状动脉人群 80 例作为正常组。

纳入标准:冠状动脉造影判定临界组与病例组的狭窄率<50.0%与≥50.0%,正常组无出现冠状动脉狭窄;病情稳定,知情同意本研究;所有人群为小学及其以上文化水平;年龄 40-80 岁。

排除标准:3 个月内曾经患有急性心肌梗死、脑血管意外或者严重创伤者;肝肾功能异常者、活动性消化道溃疡、恶性肿瘤者三组的人群一般资料对比无明显差异($P>0.05$)。见表 1。本次研究得到了医院伦理委员会的批准。

表 1 三组一般资料对比

Table 1 Comparison of the three groups of general data

Groups	n	Gender (male / female)	Age (year)	Body mass index (kg/m ²)	Heart rate (secondary / min)	Blood glucose (mmol/L)	Stenness rate (%)
Case group	80	46/34	55.25±2.15	22.48±1.83	84.92±5.50	5.38±0.11	67.39±3.16
Critical group	80	45/35	54.99±2.87	22.33±1.20	84.58±4.46	5.41±0.09	34.58±2.58
Normal group	80	47/33	55.36±3.00	22.54±1.58	84.61±5.11	5.39±0.15	-

1.2 血清前列环素、神经肽 Y 含量检测

所有人群均在清晨 8:00 之前空腹、安静状态下抽取肘静脉血 3-4 mL,待自然凝固后送检,分离血清,低温 4.0℃保存待用。采用酶联免疫法检测血清前列环素、神经肽 Y 含量,检测试剂盒都购自德赛诊断系统(上海)有限公司,严格按说明书操作。

1.3 近期预后预测

所有临界组患者预后随访到 2022 年 4 月,记录与判断患者功能性心肌缺血发生情况,判定标准:患者出现胸闷、乏力、呼吸困难、心律等症状,影像学检查出现心脏结构无明显改变。同时调查与记录临界组与病例组人群的生命质量,采用生命质量量表进行调查,包含生理维度、社会维度、心理维度、环境维度四个方面,分数越高,生命质量越高。

1.4 统计方法

采用 SPSS24.00 软件进行分析, $P<0.05$ 代表差异显著。计量数据以均数±标准差表示,计数数据以百分比、n(%)等表示,两两对比为 t 检验与卡方分析,多组间对比采用方差检验,同时进行 Pearson 相关性分析与多因素 logistic 回归分析,预测价

值分析采用接收者操作特征 (Receiver operating characteristic curve, ROC) 曲线分析,检验水准为 $\alpha=0.05$ 。

2 结果

2.1 血清前列环素、神经肽 Y 含量对比

病例组、临界组的血清前列环素含量低于正常组,血清神经肽 Y 含量高于正常组,病例组与临界组对比有明显差异($P<0.05$)。见表 2。

2.2 生命质量评分对比

病例组、临界组的生理维度、社会维度、心理维度、环境维度等生命质量评分明显低于正常组,病例组也低于临界组($P<0.05$)。见表 3。

2.3 相关性分析

在 240 例人群中,Pearson 相关性分析显示血清前列环素、神经肽 Y 含量与冠状动脉临界病变的发生存在相关性($P<0.05$)。见表 4。

表 2 三组血清前列环素、神经肽 Y 含量对比(ng/L, 均数±标准差)

Table 2 Comparison of three groups of serum prostacyclin and neuropeptide Y content (ng/L, mean ± standard deviation)

Groups	n	Prostacyclin	Neuropeptide Y
Case group	80	51.42±3.69 ^{ab}	230.18±15.29 ^{ab}
Critical group	80	61.47±4.55 ^a	188.37±19.52 ^a
Normal group	80	74.56±3.22	124.29±19.33
F		16.742	21.555
P		<0.001	0.000

Note: Compared with the normal group, ^a*P*<0.05; Compared with critical group, ^b*P*<0.05, the same as below.

表 3 三组生命质量评分对比(分, 均数±标准差)

Table 3 Comparison of quality of life scores of the three groups (score, mean± standard deviation)

Groups	n	Physiological dimension	Social dimension	psychological dimension	Environmental dimension
Case group	80	76.87±5.10 ^{ab}	77.08±4.17 ^{ab}	78.15±5.87 ^{ab}	74.60±6.19 ^{ab}
Critical group	80	84.68±5.18 ^a	83.59±5.10 ^a	84.28±5.10 ^a	84.09±5.18 ^a
Normal group	80	92.11±3.28	90.74±4.14	91.09±3.57	93.02±1.85
F		14.333	15.026	16.721	14.582
P		0.000	0.000	0.000	0.000

表 4 前列环素、神经肽 Y 与冠状动脉临界病变的相关性(n=240)

Table 4 Correlation between prostacyclin and neuropeptide Y and critical coronary artery lesions (n=240)

Indexs	Prostacyclin	Neuropeptide Y
r	-0.652	0.714
P	0.000	0.000

2.4 影响因素分析

神经肽 Y 为导致冠状动脉临界病变发生的重要因素(*P*<0.05)。

在 240 例人群中,多因素 logistic 回归分析显示前列环素、见表 5。

表 5 脂联素和超敏 C 反应蛋白与急性冠脉综合征的相关性(n=240)

Table 5 Correlation between adiponectin and hypersensitivity C-reactive protein and acute coronary syndrome (n=240)

Variables	β	P	OR	The 95% Confidence interval Upper limit-Lower limit
Prostacyclin	0.923	0.002	2.516	1.185-5.362
Neuropeptide Y	0.596	0.001	0.568	0.349-0.814

2.5 功能性心肌缺血发生情况

所有临界组患者预后随访到 2022 年 4 月,平均随访时间为 31.02±2.58 个月,发生功能性心肌缺血 21 例,发生率为 26.3%。ROC 曲线分析显示血清前列环素、神经肽 Y 预测功能性心肌缺血的曲线下面积分别为 0.828、0.836。见图 1。

3 讨论

冠状动脉临界病变当前在临床上较常见,具有一定的自限性,但处理不及时将导致冠状动脉病变^[10]。临床研究显示,冠状动脉临界病变患者 1 年后发生冠状动脉病变约为 15.0%左右,3 年后的递增至 25.0%左右,4 年后的可高达 40.0%左右^[11,12]。冠状动脉临界病变的病理生理机制为:在冠状动脉粥样硬化的基础上,使血小板聚集性增强,迅速形成血小板性血栓及纤维

素性血栓,从而引发疾病^[13]。发病因素除了包括高血压、高脂血症、糖尿病、吸烟、肥胖等原因诱发外,约有 50.0%的患者发病前无先兆表现,也无高血压、冠心病等基础病史,只是这些患者生活方式大都不健康,长期处于紧张的工作和竞争的压力下,吸烟酗酒,生活、饮食不规律,身体时常处于疲劳状态,这些均为导致冠状动脉临界病变的最大隐患^[14,15]。本研究显示病例组、临界组的血清前列环素含量低于正常组,血清神经肽 Y 含量高于正常组,病例组与临界组对比有差异;病例组、临界组的生理维度、社会维度、心理维度、环境维度等生命质量评分明显低于正常组,病例组也低于临界组,表明冠状动脉临界病变患者多伴随有前列环素、神经肽 Y 表达异常,可导致生命质量下降。分析可知,前列环素具有能抑制血小板功能,减少凝血酶及血小板衍生的生长因子等促血栓形成,还具有抑制血小板聚集

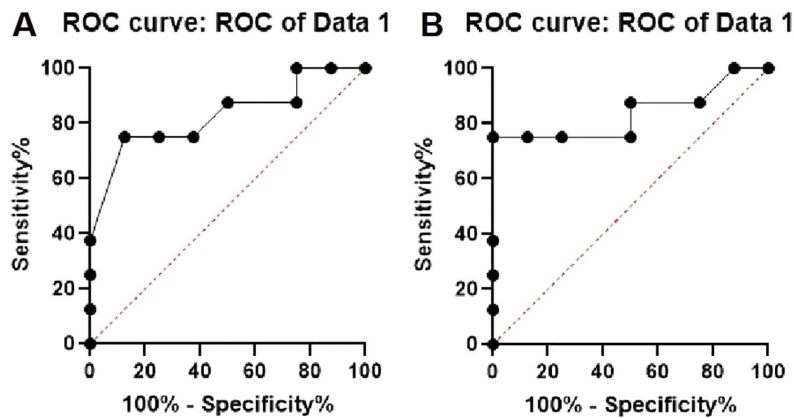


图1 血清前列环素、神经肽 Y 预测冠状动脉临界病变功能性心肌缺血的曲线下面积

Fig. 1 Area under the curve of serum prostacyclin and neuropeptide Y predicting functional myocardial ischemia in critical coronary artery lesions

的作用冠状动脉临界病变患者可伴随有交感神经兴奋,可使得儿茶酚胺等活性物质分泌增加,可导致前列环素分泌减少^[16,17]。神经肽 Y 是一种心血管系统中含量非常丰富的神经肽,可通过多种途径参与心血管功能的调节,于交感神经的胞体内合成。神经肽 Y 具有收缩冠状动脉、兴奋交感神经、损伤血管内皮等作用,参与了冠状动脉临界病变的发病过程^[18,19]。

血栓形成是冠状动脉临界病变发生的主要病理生理基础,而冠脉痉挛在冠状动脉临界病变的发生、发展过程中也发挥着重要作用^[20]。本研究显示 Pearson 相关性分析显示血清前列环素、神经肽 Y 含量与冠状动脉临界病变的发生存在相关性;多因素 logistic 回归分析显示前列环素、神经肽 Y 为导致冠状动脉临界病变发生的重要因素,表明前列环素、神经肽 Y 与冠状动脉临界病变存在相关性。董小伟等人^[21]的研究发现:血浆 PGI₂ 水平下降和 NPY 水平升高与糖尿病肾病患者心血管病变有关,二者联合预测心血管不良事件发生的效能较好,与本研究结果具有一致性。分析可知:前列环素可通过间接抑制巨噬细胞向泡沫细胞的转变,降低巨噬细胞内胆固醇的含量,减弱动脉血栓形成过程在斑块稳定性方面起作用。此外,其本身尚具有膜稳定作用,能阻止细胞内外离子的异常分布,保证线粒体合成 ATP 的功能,避免钙离子超负荷。其低表达可增加氧化损伤,引起膜流动性降低和通透性增高,导致冠状动脉病变的发生^[22,23]。血清神经肽 Y 可直接作用血管平滑肌节受体引起血管收缩,抑制神经肽 Y 的表达,可促进释放乙酰胆碱,引起冠状动脉痉挛,加重心肌缺血^[24]。其浓度增加引起冠脉血管痉挛可能是冠状动脉临界病变发生发展的重要病理生理基础之一,浓度减少可有效缓解胸痛和缺血症状,纠正交感神经过度兴奋,促进改善患者的预后。在临床上冠状动脉临界病变的发生率远高于冠状动脉病变。更值得注意的是,神经肽 Y 为一种氨基酸多肽,可参与调节机体的焦虑、抑郁、学习、记忆,抑制呼吸等过程。神经肽 Y 有直接收缩血管的作用,是体内血管收缩物质之一,能减少冠状动脉的血流供应,造成血管内皮细胞的损伤^[24-27]。

本研究显示所有临界组患者预后随访到 2022 年 4 月,平均随访时间为 31.02±2.58 个月,发生功能性心肌缺血 21 例,发生率为 26.3 %。ROC 曲线分析显示血清前列环素、神经肽 Y

预测功能性心肌缺血的曲线下面积分别为 0.828、0.836。冠状动脉粥样硬化斑块破裂、血栓形成是冠状动脉病变发生的主要病理生理基础,在其发病早期多表现为冠状动脉临界病变^[28]。神经肽 Y 是一种强力的缩血管活性肽,交感神经兴奋时二者可同时释放,可参与多种心血管疾病的发生与发展。前列环素的低表达可使细胞膜脂质过氧化损伤进一步加重,促使大量钙内流,改变膜流动性和通透性,使质膜与肌浆网膜的钙泵失灵,导致线粒体功能障碍,ATP 生成减少,加重细胞内钙超载^[29]。当冠状动脉临界病变患者在严重缺血和剧烈胸痛等刺激下交感神经过度兴奋,致神经肽 Y 释放增加,可通过激活补体系统促进动脉粥样硬化形成,从而导致患者病情恶化^[30]。本研究存在一定不足,调查人数比较少,也未预测患者的其他心血管疾病发生情况,将在后续进行更深入研究。

总之,冠状动脉临界病变患者多伴随有前列环素、神经肽 Y 表达异常,可导致生命质量下降,前列环素、神经肽 Y 与冠状动脉临界病变存在相关性,两者预测近期功能性心肌缺血的发生具有很好的价值。

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