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急性冠脉综合征患者发生冠脉血管完全闭塞病变的影响因素分析*

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摘要 目的 探讨急性冠脉综合征(acute coronary syndrome ACS)患者发生冠脉血管完全闭塞病变的影响因素。方法 从2013年在我院诊断为ACS且行冠状动脉造影检查患者中随机筛选出120例患者为研究对象,记录其基线及临床资料,回顾其造影图像,计算SYNTAX积分,根据是否存在完全闭塞病变分组,分析慢性完全闭塞病变的影响因素。结果 与不完全闭塞病变组相比,完全闭塞病变组吸烟(61.1% P=0.041)、糖尿病(35.2% P=0.025)、高脂血症(55.6% P=0.033)发生率高,入院静息心率(77.07±11.99, P=0.023)高,中性粒细胞/淋巴细胞比值(Neutrophil-to-Lymphocyte Ratio NLR)水平(8.69±9.46 P<0.001)显著升高,左室射血分数(left ventricular ejection fraction, LVEF)(50.39±8.36 P=0.001)显著降低。多因素分析显示年龄(P=0.043)、急性心肌梗死(acute myocardial infarction AMI)的发生(P=0.003)、LVEF(P=0.002)、NLR(P=0.002)、脂蛋白(a)(P=0.039)、SYNTAX积分(P=0.002)和完全闭塞病变独立正相关。结论 ACS患者发生慢性完全闭塞病变与年龄、静息心率、吸烟史、高脂血症相关,与冠脉病变复杂程度、左室功能下降密切相关。NLR作为新型炎症标志之一,可预测ACS患者完全闭塞病变。

关键词 中性粒细胞/淋巴细胞比值 急性冠脉综合征 完全闭塞病变

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Study on the Relationship between Neutrophil-to-lymphocyte Ratio with Totally Occluded Lesion*

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ABSTRACT Objective: To explore the influencing factors of totally occluded lesion in coronary artery in acute coronary syndrome.

Methods: One hundred and twenty patients from the cardiology intervention treatment center of General Hospital of Chinese People's Liberation Army who were diagnosed with acute coronary syndrome(ACS) and underwent coronary angiography were randomly selected as objects of study. The clinical data was obtained from the medical records. Reviewed the angiographic images and calculated the SYNTAX score. Divided the cases into two groups according to the existence of totally occluded lesion, then analysed the influencing factors of chronic total occlusion of coronary artery. **Results:** Compared with non-totally occluded lesion group, there existed high incidence of smoking(61.1%, P=0.041), diabetes(35.2%, P=0.025) and hyperlipidemia(55.6%, P=0.033) in the totally occluded lesion group, but also resting heart rate in hospital(7.07±11.99, P=0.023) and NLR levels(8.69±9.46, P<0.001) were significantly higher in the totally occluded lesion group; whereas LVEF (50.39±8.36, P=0.001) decreased significantly. In the multivariable regression analysis, there was a positive correlation among age(P=0.043), acute myocardial infarction(AMI)(P=0.003), LVEF(P=0.002), NLR(P=0.002), Lipoprotein(a)(P=0.039), SYNTAX SCORE (P=0.002) and chronic total occlusion. **Conclusion:** In patients with ACS, chronic total occlusion is closely related with age, resting heart rate, smoking and hyperlipidemia, as well as complexity of coronary artery lesions, decreased left ventricular function. As a new type of the inflammation biomarkers, NLR may predict chronic total occlusion in acute coronary syndrome.

Key words: Neutrophil-to-lymphocyte ratio; Acute coronary syndrome; Chronic total occlusion

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前言

动脉粥样硬化是以脂质和纤维在大动脉的累积为特点的

发展性疾病,是增加心血管疾病风险最重要的因素^[1]。炎症与内皮功能失调引发动脉管壁的粥样硬化进展导致机体器官血供减少,引起住院率及死亡率增加^[2-4]。急性冠脉综合征(ACS)是心

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内科及急诊科常见的急症,易发生心血管不良事件,致生活质量下降,病死率高。慢性完全闭塞病变往往与冠脉病变的复杂程度正相关,血管再通率低,患者预后差。因为高风险虽慢性闭塞病变常见但病变处理相对较少^[23]。

中性粒细胞/淋巴细胞比值(NLR)作为两种特定白细胞亚型的结合在近年来多项研究中脱颖而出。NLR是机体系统炎症的标志之一,研究发现其与稳定性心绞痛、不稳定性心绞痛、急性失代偿性心衰的死亡等心源性不良事件的发生相关^[5,6]。本研究旨在探究ACS发生慢性完全闭塞病变的影响因素。

1 资料和方法

1.1 临床资料

从2013年在我院诊断为ACS且行冠状动脉造影检查的患者中随机筛选出120例患者,记录其基线及临床资料,计算NLR。急性冠脉综合征包括不稳定心绞痛和AMI(可分为非ST段抬高型心肌梗死、ST段抬高型心肌梗死)。2007年欧洲慢性完全闭塞病变俱乐部将慢性完全闭塞病变定义为冠脉造影检查闭塞血管段前向血流TIMI 0级,且闭塞时间至少3个月。排除标准:①曾接受过经皮冠状动脉介入术、冠状动脉旁路移植术、瓣膜置换或修补术或心脏移植手术者;②LVEF<40%,或者有严重心力衰竭症状,或者心源性休克;③急性感染、创伤或手术后2周内;④急性感染或慢性炎症改变;⑤肝胆疾病活动期、严重肝、肾功能衰竭(CKD4-5期);⑥血液系统疾病、风湿类或免疫系统疾病、或近期接受类固醇类药物治疗的患者;⑦恶性肿瘤,或合并全身其他脏器疾病、预期寿命<1年。

1.2 方法

所有患者入院时均采血常规化验,根据血常规化验获得数据,按中性粒细胞淋巴细胞比值计算NLR,根据是否存在完全闭塞病变分为2组。其余基线资料、血液化验项目、检查项目、冠脉造影情况根据住院病历收集记录。SYNTAX评分根据冠脉造影通过专业软件计算。分析NLR与慢性完全闭塞病变的相关性。

1.3 统计学处理

采用SPSS19.0软件进行统计学分析,计量资料采用均数±标准差表示,两组间比较采用t检验;不符合正态性或方差齐性的计量资料采用秩和检验;计数资料用百分比(%)表示,采用 χ^2 检验,以P<0.05为差异有统计学意义。

2 结果

2.1 两组基本临床资料的比较

本研究共纳入118例患者,其中2例失访。无完全闭塞病变组64例,平均年龄(60.60±9.78)岁;完全闭塞病变组54例,平均年龄(57.11±12.00)岁。两组均以男性患者居多,但两组比较无明显差异。完全闭塞病变组心梗患者所占比例明显高于无完全闭塞病变组,吸烟、糖尿病、高脂血症患者所占比例高于无完全闭塞病变组,入院后静息心率高于完全闭塞病变组,差异均有统计学意义(P<0.05)。而BMI、既往心梗及脑梗病史、高血压及其数值、冠心病家族史在两组间比较差异均无统计学意义(P>0.05),见表1。

表1 两组患者一般临床资料比较(例,%)

Table 1 The comparison of basic and clinical data between two groups (n, %)

Items	Chronic total occlusion		P
	N(n=64)	Y(n=54)	
Age(year)	60.60± 9.78	57.11± 12.00	0.118
Gender(male)	42(65.6)	42(77.8)	0.146
BMI	25.56± 3.07	25.80± 3.52	0.755
Heart rate(beats/ min)	72.25± 8.50	77.07± 11.99	0.023
Smoking	27(42.2)	33(61.1)	0.041
Previous MI	8(12.5)	5(9.3)	0.575
Previous cerebral infarction	10(15.6)	6(11.1)	0.476
Hypertension	31(48.4)	32(59.3)	0.240
SBp(mmHg)	160± 22.5	170± 40	0.180
DBp(mmHg)	100± 12.5	100± 15	0.505
Hyperlipidemia	23(35.9)	30(55.6)	0.033
Diabetes melitus	11(17.2)	19(35.2)	0.025
Family history	17(26.6)	16(29.6)	0.712
AMI	23(35.9)	36(66.7)	0.001

2.2 两组左室功能、实验室指标、SYNTAX积分的比较

与无完全闭塞病变组相比,完全闭塞病变组LVEF更低,中性粒细胞百分值更高、淋巴细胞百分值更低、NLR比值更高,脂蛋白(a)更高,差异均有统计学意义(P<0.05)。用SYNTAX积分评估冠脉复杂程度,发现完全闭塞病变组评分显著高于无完全闭塞病变组(P<0.05)。而血小板平均体积、高敏C反应蛋

白、胆红素、肌酐、尿酸、胆固醇及甘油三酯在两组间比较差异均无统计学意义(P>0.05)。见表2。

2.3 ACS患者发生完全闭塞病变的影响因素

经多因素logistic回归发现年龄、心梗的发生、LVEF、NLR、脂蛋白(a)及SYNTAX积分是ACS患者发生完全闭塞病变的危险因素,见表3。

表 2 两组间左室功能、实验室指标、SYNTAX 积分的比较

Table 2 Comparison of the LVEF, laboratory parameters and SYNTAX score between two groups

Items	Chronic total occlusion		P
	N(n=64)	Y(n=54)	
LVEF (%)	56.53± 8.46	50.39± 8.36	0.001
LVEDD(mm)	44.45± 4.71	45.98± 5.03	0.145
Neutrophil(%)	0.60± 0.14	0.76± 0.16	0.000
Lymphocyte(%)	0.31± 0.12	0.19± 0.13	0.000
The average of NLR	3.20± 4.66	8.69± 9.46	0.000
Mean platelet volume(fl)	10.74± 0.93	10.50± 1.00	0.224
CRP(mg/dl)	0.38± 0.59	0.52± 0.90	0.430
Total bilirubin(μmol/L)	10.31± 4.90	11.52± 5.32	0.259
Direct bilirubin(μmol/L)	3.13± 1.67	3.51± 1.76	0.303
Creatinine(μmol/L)	74.54± 32.23	74.84± 25.79	0.913
Uric acid(μmol/L)	312.31± 82.38	322.99± 84.21	0.536
TC(mmol/L)	4.32± 1.01	4.50± 0.89	0.451
TG(mmol/L)	1.32± 1.03	1.16± 0.94	0.209
HDL(mmol/L)	1.04± 0.26	1.07± 0.16	0.521
LDL(mmol/L)	2.62± 0.84	2.93± 0.77	0.112
Lipoprotein(a)(mg/dl)	13.55± 9.93	21.53± 11.51	0.033
SYNTAX	10.3 ± 6.8	19.2 ± 7.6	0.000

表 3 完全闭塞病变的影响因素

Table 3 Influencing factors of chronic total occlusion

Items	β ± SE	Wald	P
Age	-0.221± 0.102	3.964	0.043
AMI	1.284± 0.442	8.896	0.003
Heart rate(beats/ min)	0.038± 0.02	3.251	0.076
LVEF	-0.086± 0.032	9.523	0.002
NLR	0.145± 0.053	9.889	0.002
Lipoprotein(a)(mg/dl)	0.059± 0.030	3.975	0.039
SYNTAX	0.042± 0.027	9.987	0.002

3 讨论

动脉粥样硬化是多因素参与的炎症性疾病,特点是低程度动脉炎症,随疾病进展而发展^[7]。既往的流行病学及临床研究显示外周淋巴细胞计数和冠心病患者不良心血管事件的发生显著相关^[6]。NLR 是严重动脉粥样硬化的预测因子,可能用于心血管风险分层^[8]。一些研究提出高 NLR 和心血管疾病如稳定性心绞痛、ACS 及经介入或搭桥的不良结局相关^[9-12]。既往研究表明慢性完全闭塞病变在 ACS 患者中多见,约占 1/3,是冠状动脉粥样硬化的晚期阶段,多合并多支病变,病变复杂,合并吸烟、糖尿病、高血压者心血管不良事件发生风险成倍增加^[13]。在介入治疗时病变复杂且困难,需要专业团队有熟练的技巧,较长手术时间及较大剂量造影剂,且患者需承担高手术风险:如冠状动脉穿孔,对比剂肾病,过量辐射暴露及损伤侧支循环^[24,25]。

慢性闭塞病变由血栓阻塞整个动脉管腔发展而来,紧随的是血栓机化和不同程度的血栓再通,这些过程都是临床上静止的。血栓机化的过程和由炎症细胞伴行的管腔内新生微血管同时发生,进一步则是平滑肌细胞渗透和蛋白多糖基质的沉积^[15]。

慢性闭塞病变的发生发展阶段中均可见细胞炎症和管壁新生血管之间紧密关系^[16],可见炎症与慢性完全闭塞病变紧密相关。2014 年 Demir 等^[14]研究发现 NLR 在慢性闭塞病变中显著升高,NLR 检测慢性闭塞病变的特异度为 69.3%,敏感度为 61%。本研究结果也显示升高的 NLR 与慢性完全闭塞病变显著相关。

冠脉侧支循环是主支血管闭塞后的适应性反应,可保护损伤或缺血的组织,从而减轻心绞痛症状及减少心血管不良事件。一项关于慢性闭塞病变的研究用反射波增强指数(AIx)(27.3± 8.9 vs 18.7± 7.4, P<0.001)和脉搏波传导速度(PWV)(11.7± 2.6 vs 8.5± 1.4, P<0.001)发现贫瘠的侧支循环和动脉僵硬度独立相关,高 NLR 和贫瘠侧支循环显著相关^[17]。经冠脉造影证实侧支循环贫瘠的稳定性冠心病病人 NLR 比侧支循环丰富者显著升高(4.2± 2.8 vs 3± 3.1, P=0.001)。多元回归分析显示 NLR(OR=1.199)和血清甘油三酯水平(OR=1.006)是较差侧支循环的独立预测因子^[18]。另外,我们发现入院时冠脉存在闭塞病变的患者静息心率较高,这可能是由于长时间心肌缺血或坏死导致心脏收缩功能下降,可能以提高心率来达到较大心输出

量。

SYNTAX 积分是能客观评估冠脉病变严重性的解剖学工具,可指导搭桥及介入手术的选择,其根据病变严重性、解剖学位置、供血范围评估冠脉病变段的严重性。有研究报道升高的炎症标志和白细胞计数和冠心病的严重程度相关^[19]。在经冠脉重建的患者中,高 SYNTAX 已被用来预测不良短期及长期临床结局^[20]。研究表明用 SYNTAX 评估稳定性冠心病,发现 NLR 和冠心病的复杂及严重程度相关^[21],冠心病患者高 NLR 和 SYNTAX 评估的严重冠脉病变独立相关^[22]。

总之,NLR 是一个炎症标志,也可作为一个新兴、简易的心血管风险指标成为冠心病危险因素评分及危险分层的重要指标。但目前对于 NLR 的分组截点值不统一,需要进一步研究探讨。本研究探究了 NLR 和慢性闭塞病变之间的关系。在完全闭塞病变组 NLR 水平明显升高,提示高 NLR 水平预测冠心病中完全闭塞病变病人。

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