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冠心病患者经皮冠状动脉介入治疗术后支架内再狭窄的相关危险因素分析*

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摘要 目的:探究冠心病(CHD)患者经皮冠状动脉介入治疗(PCI)术后支架内再狭窄(ISR)的相关危险因素。**方法:**选取2014年6月~2017年6月期间我院收治的行PCI的CHD患者200例为研究对象,术后随访一年再行冠脉造影检测,根据患者是否发生ISR分为观察组(38例,发生ISR)和对照组(162例,未发生ISR),收集并比较两组患者基线资料及生化指标,采用多因素logistic回归分析CHD患者PCI术后发生ISR的危险因素。**结果:**观察组吸烟、饮酒、高血压、糖尿病的人数占比、病程及支架直径均高于对照组,差异有统计学意义($P<0.05$)。观察组脂蛋白(a)[LP(a)]、纤维蛋白原(FIB)及尿酸(UA)水平显著高于对照组,总胆红素(TBIL)水平显著低于对照组,差异有统计学意义($P<0.05$)。多因素logistic回归分析显示,吸烟、糖尿病、支架直径(小)以及高水平LP(a)、低水平UA为CHD患者行PCI术后发生ISR的危险因素。**结论:**CHD患者行PCI术后发生ISR的危险因素有吸烟、糖尿病、支架直径以及高水平LP(a)、低水平UA,因此在PCI术中应尽可能选用较大的支架,同时戒烟、控制血糖有利于预防ISR的发生,定期检测血清LP(a)、UA水平变化,并采取有效的医疗与保健措施能够减少ISR的发生风险。

关键词:冠心病;冠状动脉介入治疗;支架内再狭窄;危险因素

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Risk Factors for in Stent Restenosis after Percutaneous Coronary Intervention in Patients with Coronary Heart Disease*

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ABSTRACT Objective: To explore the risk factors of in stent restenosis (ISR) after percutaneous coronary intervention (PCI) in patients with coronary heart disease (CHD). **Methods:** 200 patients with CHD undergoing percutaneous PCI in our hospital from June 2014 to June 2017 were selected as subjects. Coronary angiography was performed after one year follow-up. The patients were divided into observation group (38 cases with ISR) and control group (162 cases without ISR) according to whether the patients had ISR. The baseline data and biochemical indicators were collected and compared between the two groups. Multivariate logistics regression analysis was used to analyzed the risk factors for CHD in patients with PCI after ISR. **Results:** The proportion and duration of smoking, drinking, hypertension, diabetes mellitus and stent diameter in the observation group were higher than those in the control group, the differences were statistically significant($P<0.05$). The levels of lipoprotein (a) [LP (a)], fibrinogen (FIB) and uric acid (UA) in the observation group were significantly higher than those in the control group, the level of total bilirubin (TBIL) was significantly lower than that of the control group, the differences were statistically significant ($P<0.05$). Multivariate logistic regression analysis showed that smoking, diabetes mellitus, stent diameter (small), higher level of LP (a) and lower level of UA were risk factors for ISR after PCI in patients with CHD. **Conclusion:** The risk factors of ISR in CHD patients after PCI are smoking, diabetes mellitus, stent diameter (small), higher level of LP (a) and lower level of UA. Therefore, large scaffolds should be used as far as possible in PCI, at the same time, giving up smoking and controlling blood sugar are good for preventing the occurrence of ISR. Serum levels of LP (a) and UA are measured regularly, and taking effective medical and health care measures can reduce the risk of ISR.

Key words: Coronary heart disease; Percutaneous coronary intervention; In stent restenosis; Risk factors

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前言

冠心病(Coronary heart disease, CHD)是指机体冠状动脉出现粥样硬化并引起血管狭窄或堵塞,从而造成血管供血不足,病变处心肌缺血、缺氧,进而导致心脏结构重塑的一类疾病^[1]。研究显示^[2,3],随着社会发展及人们物质生活水平的提高,我国居民行为生活方式发生了较大改变,近年来 CHD 的发病率及死亡率呈现逐年升高趋势,对居民的生命健康产生严重影响。既往冠脉搭桥术是治疗 CHD 的常见方法,但有报道显示,经冠脉搭桥术治疗后患者易复发,易发生血管再狭窄、闭塞,一年内支架内再狭窄(In stent restenosis, ISR)发生率可达 15%^[4],而且随着时间的推移,患者冠脉病变的程度会加重,未病变处的冠脉及其桥血管也易发生病变,因此,再行冠脉搭桥治疗的成功率较低。有研究显示^[5,6],经皮冠状动脉介入治疗(Percutaneous coronary intervention, PCI)在重建患者血运上具有明显效果,但仍存在发生 ISR 的风险。因此,本研究通过探究 PCI 术后患者 ISR 发生的危险因素,为临床 CHD 患者 PCI 术后更好的指导康复,防止 ISR 发生提供理论依据,现报告如下。

1 资料与方法

1.1 一般资料

选择我院于 2014 年 6 月~2017 年 6 月期间收治的行 PCI 的 CHD 患者 200 例为研究对象。纳入标准:① 所有患者在术前均经冠脉造影确诊为 CHD;② 临床资料完整;③ 术后均按医嘱服药,依从性较高;④ 所有患者及其家属对本研究均知情同意。排除标准:① 存在严重心律失常、心源性晕厥、心源性休克病史者;② 合并严重免疫系统疾病及肿瘤者;③ 合并肝、肾功能不全者;④ 冠脉造影不清、冠脉造影禁忌症者及中途因退出者;200 例患者中,男 129 例,女 71 例,年龄 50~80 岁,平均年龄(62.24±6.19)岁;所有患者术后均随访一年,再行冠脉造影,根据其是否发生 ISR 分为观察组和对照组,其中,观察组 38 例患者为发生 ISR 者,表现为支架置放处冠脉狭窄达 50%及以上;对照组 162 例为未发生 ISR 者,表现为冠脉支架置放处狭窄低于 50%。本研究所有操作均符合医学伦理学道德,并通过我院伦理委员会审核。

1.2 研究方法

1.2.1 治疗方法 所有患者均行冠状动脉造影,根据造影结果行 PCI 置入支架,手术均获得成功,术后冠脉残余狭窄均低于 30%,无严重并发症,前向血流心肌梗死溶栓治疗 TIMI 血流分级为 3 级。术后患者均服用氯吡格雷 75 mg/d、阿司匹林 100 mg/d,置入药物涂层支架患者服药 12 月,置入裸支架患者服用 6 个月。

1.2.2 资料收集 收集所有患者以下几方面内容:(1) 基线资料:性别、年龄、饮酒史、吸烟史、糖尿病、高血压、高脂血症疾病史、CHD 病程、PCI 史、本次 PCI 植入支架的直径、数量及长度等;(2) 生化指标:在所有患者 1 年后行冠状动脉造影的次日,收集清晨空腹肘静脉血 5 mL,室温置于 3000 rpm 离心机离心 30 min,取上层血清,采用 HITACHI7600-110E 全自动生化分析仪测定总甘油三酯(Total triglyceride, TG)、总胆固醇(Total cholesterol, TC)、高密度脂蛋白胆固醇(High density lipoprotein

cholesterol, HDL-C)、低密度脂蛋白胆固醇(Low density lipoprotein cholesterol, LDL-C)、脂蛋白(a)[Lipoprotein, Lp(a)]、谷丙转氨酶(Glutamic pyruvic transaminase, ALT)、谷草转氨酶(Glutamic pyruvic transaminase, AST)、总胆红素(Total bilirubin, TBIL)、肌酐(Creatinine, Cr)、尿素氮(Urea nitrogen, BUN)、纤维蛋白原(Fibrinogen, FIB)、尿酸(Uric acid, UA)水平。

1.3 统计学分析

应用 SPSS20.0 统计学软件进行数据分析,计量资料以均数±标准差表示,比较采用 t 检验;计数资料以率或百分比表示,比较采用 χ^2 检验;采用多因素 logistic 回归方法对 CHD 患者行 PCI 术后发生 ISR 的危险因素进行分析,以 $P<0.05$ 表示差异有统计学意义。

2 结果

2.1 两组患者基线资料比较

两组患者性别、年龄、高脂血症人数占比、PCI 既往史、支架数量与长度比较,差异无统计学意义($P>0.05$);观察组吸烟、饮酒、高血压、糖尿病的人数占比、病程及支架直径均显著高于对照组,差异有统计学意义($P<0.05$),见表 1。

2.2 两组患者生化指标情况比较

观察组患者 Lp(a)、FIB 及 UA 水平显著高于对照组, TBIL 水平显著低于对照组,差异均均有统计学意义($P<0.05$);两组患者 TG、TC、LDL-C、HDL-C、ALT、AST、Cr 及 BUM 水平比较,差异无统计学意义($P>0.05$),见表 2。

2.3 CHD 患者行 PCI 术后发生 ISR 的危险因素分析

将 2.1、2.2 中差异有统计学意义的变量纳入多因素 logistic 回归模型分析,变量筛选采用逐步回归,结果显示:吸烟、糖尿病、支架直径(小)以及高水平 Lp(a)、低水平 UA 为 CHD 患者行 PCI 术后发生 ISR 的危险因素。

3 讨论

随着我国经济的发展、人们生活水平的提高及老年化进程的加快,近年来我国 CHD 的发生率呈现逐年上升趋势^[7]。研究显示^[8],我国现存 CHD 患者超过 2000 万,其可导致心绞痛、梗死及猝死等并发症,严重威胁患者生命安全。自 1986 年开展 PCI 手术治疗 CHD 后,PCI 技术在我国迅速发展,已成为治疗 CHD 患者重建血运的有效措施,但术后 ISR 的发生始终是困扰医生与患者的一个难题^[9]。由于 PCI 术后,患者机体血管内皮细胞受到损伤,血管内膜也将发生增生,导致患者血管重塑弹性下降^[10],同时 CHD 患者本身血管易发生血栓以及炎性反应,从而加大了 ISR 的发生风险^[11],因此,分析 CHD 患者 PCI 术后发生 ISR 的具体危险因素具有重要的临床意义。

既往多项研究显示^[12-14],吸烟是心脑血管疾病发生的危险因素,其不仅可以降低血管 HDL-C 浓度,增加机体内细胞黏性,而且还能够促进细胞聚集,损伤动脉内皮。本研究显示,观察组患者吸烟率显著高于对照组,多因素结果也显示,吸烟是引发术后 ISR 发生的危险因素,说明吸烟可以影响患者 PCI 术后 ISR 的发生。分析其原因可能与烟草中含有可氧化血管内自由基引起血管损伤,促使血管内皮过度增生的一氧化碳、煤焦油等有害物质相关,与王冬梅、刘宁等报道结果一致^[15,16],因此,

表 1 两组患者治疗前一般情况比较

Table 1 Comparison of general conditions before treatment between the two groups

Indexes	Observation group(38 cases)	Control group(162 cases)	t/χ^2	<i>P</i>
Sex (male/female)	25/13	104/58	0.143	0.887
Age (years)	62.61± 5.84	61.99± 6.39	0.314	0.734
Smoking(%)	16(42.11)	32(19.75)	6.384	0.000
Drinking(%)	13(34.21)	30(18.52)	5.382	0.000
Hypertension(%)	29(76.32)	89(54.94)	4.121	0.001
Diabetes mellitus(%)	15(39.47)	29(17.90)	5.1663	0.000
Hyperlipidemia(%)	11(28.95)	33(20.37)	0.837	0.313
Course of disease (years)	9.63± 2.73	6.89± 2.38	3.922	0.001
Past history of PCI	5(13.16)	10(6.17)	0.362	0.653
Number of stents(number)	1.93± 0.89	1.87± 0.91	0.225	0.768
Stent diameter(mm)	2.87± 0.29	3.21± 0.42	2.831	0.004
Bracket length(mm)	45.43± 12.31	37.20± 13.28	1.789	0.057

表 2 两组患者生化指标比较($\bar{x} \pm s$)

Table 2 Comparison of biochemical indexes between two groups($\bar{x} \pm s$)

Indexes	Observation group(38 cases)	Control group(162 cases)	<i>t</i>	<i>P</i>
TG(mmol/L)	2.12± 1.10	1.78± 1.25	1.572	0.091
TC(mmol/L)	3.80± 1.22	3.56± 0.89	1.233	0.214
LDL-C(mmol/L)	2.09± 0.76	1.99± 0.93	1.321	0.193
HDL-C(mmol/L)	0.99± 0.32	1.02± 0.28	0.982	0.334
LP(a)(g/L)	0.51± 0.39	0.37± 0.23	4.213	0.000
ALT(U/L)	24.79± 17.39	23.10± 13.75	0.893	0.341
AST(U/L)	27.91± 13.23	23.73± 12.66	0.726	0.456
TBIL(μmol/L)	10.79± 2.37	12.83± 2.16	2.563	0.012
Cr(μmol/L)	72.39± 17.33	74.15± 15.39	0.613	0.563
BUM(mmol/L)	5.36± 1.03	5.56± 1.23	1.322	0.183
FIB(g/L)	2.98± 0.34	2.69± 0.53	2.637	0.008
UA(μmol/L)	397.22± 67.39	351.28± 56.82	2.889	0.005

表 3 CHD 患者行 PCI 术后发生 ISR 的 logistic 回归分析

Table 3 Logistic regression analysis of ISR after PCI in patients with CHD

Indexes	β	S.E	OR	Wald χ^2	<i>P</i>	95%IC	
						Lower	Upper
Smoking	1.332	0.632	3.331	6.764	0.010	1.925	8.337
Diabetes mellitus	1.031	0.817	2.631	5.341	0.021	1.431	5.573
Stent diameter	0.563	0.273	0.773	5.738	0.014	0.668	0.893
LP(a)	1.632	0.772	2.134	8.428	0.001	1.371	4.381
UA	0.661	0.198	1.993	6.323	0.014	1.288	4.116

患者 PCI 术后应该严格禁烟以预防 ISR 的发生。本研究显示, 合并有糖尿病的 CHD 患者 PCI 术后发生 ISR 的危险性是非糖尿病的 2.631 倍, 分析其原因为: 一方面糖尿病患者自身存在

炎性血管损失和血管内皮细胞损伤^[17,18], 另一方面糖尿病患者机体血栓素 A2 合成增多, 而血栓素 A2 可促进血管收缩, 减少血管舒张因子前列环素的合成, 从而抑制血管舒张, 激活血小

板聚集,造成血管狭窄,与既往报道一致^[19,20]。本研究显示,植入支架的直径较小是再生ISR的危险因素,其原因主要与PCI手术特点相关,直径较小的支架主要置于较细的冠脉,此处往往血流量较少,血流阻力较大,在植入支架过程中需要的压力较大,更容易损伤血管内膜,从而易引起内膜增生,再发ISR;相反,支架直径越大对冠脉的损失会越小,可避免ISR的发生,为术后再发ISR的保护因素,与既往报道结果一致^[21]。

Lp(a)作为一种血浆脂蛋白,其胆固醇含量较高,在血管血栓形成及动脉粥样硬化的发生中扮演重要作用^[22]。本研究显示,机体高Lp(a)水平是CHD患者术后ISR发生的危险因素。分析原因为Lp(a)中载脂蛋白的基因序列与纤溶酶原的高度相似,其可引起机体免疫原性,从而导致纤溶酶原表达及活性降低,进而促使血栓形成。此外,有研究报道^[23,24],Lp(a)还可作用于肝细胞和内皮细胞分泌纤溶酶原抑制剂,促使血栓形成,从而导致患者ISR发生。既往报道^[25,26]显示,当机体内UA升高时,一方面UA可引起尿酸盐结晶生产,沉积于血管内壁导致血管损失,引起动脉粥样硬化的发生,另一方面,UA可促使血管内血小板聚集形成血栓,从而加重血管堵塞。本研究显示,CHD患者PCI术后UA水平升高是导致ISR的危险因素,与既往报道结果一致^[27]。但既往报道显示^[28-30],血管内TBIL具有抗氧化作用,可防止血管内血栓生产,在预防ISR方面具有一定作用,因此,提高机体内TBIL水平可减少CDH患者PCI术后ISR的发生。

综上所述,吸烟、糖尿病、支架直径(小)以及机体高水平的LP(a)与低水平UA是CHD患者行PCI治疗后发生ISR的危险因素,因此,在进行PCI术时,应尽可能的给患者置入较大的支架,同时患者在术后应该戒烟、控制血糖,定期检测血清LP(a)、UA水平,并有针对性的采取医疗和保健措施,以预防ISR的发生。

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