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## 血清 Scr、CysC 及 Hcy 水平预测急性冠脉综合征 PCI 术后造影剂肾病发生的价值

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**[摘要]** 目的: 血清肌酐(serum creatinine, Scr)、胱抑素C(cystatin C, CysC)及同型半胱氨酸(homocysteine, Hcy)水平预测急性冠脉综合征(acute coronary syndrome, ACS)经皮冠状动脉介入术(percutaneous coronary intervention, PCI)术后造影剂肾病(contrast-induced nephropathy, CIN)发生的价值。方法: 连续收集2018年1月至2020年3月南京医科大学附属江宁医院收治的择期行PCI手术治疗的87例ACS患者。根据患者术后是否发生CIN分为CIN组(发生CIN)和非CIN组(未发生CIN)。比较两组血清Scr、CysC及Hcy水平, 并通过多因素logistic回归分析CIN发生的相关的危险因素。此外, 绘制受试者工作特征(receiver operating characteristic curve, ROC)曲线分析血清CysC、Hcy对CIN的预测价值。结果: 87例ACS患者经PCI治疗病情均得到缓解, 术后30例发生CIN, 发生率为34.5%; CIN组吸烟、高血压、糖尿病占比均明显高于非CIN组(均 $P < 0.05$ ); CIN组术后血清Scr、CysC、Hcy水平均明显高于术前水平(均 $P < 0.05$ ), 且高于同期非CIN组水平(均 $P < 0.05$ )。两组术前血清Scr、CysC、Hcy比较差异均无统计学意义(均 $P > 0.05$ ); logistic回归分析结果显示血清CysC、Hcy为CIN发生的独立危险因素; ROC曲线显示术后48 h血清CysC、Hcy预测CIN发生的价值均较高, 其中CysC预测CIN发生的最佳临界值为1.4 mg/L, AUC为0.764(95%CI: 0.664~0.863), Hcy预测CIN发生的最佳临界值为10.2  $\mu\text{mol/L}$ , AUC为0.813(95%CI: 0.720~0.907)。结论: 血清CysC、Hcy为ACS患者PCI术后并发CIN的独立影响因素, 该类患者体内上述指标水平明显异常, 术后48 h对其进行检测可有效预测CIN发生。

**[关键词]** 肌酐; 胱抑素C; 同型半胱氨酸; 急性冠脉综合征; 经皮冠状动脉介入术; 造影剂肾病

## Value of serum SCR, CysC, and Hcy levels in predicting the occurrence of contrast nephropathy after PCI in acute coronary syndrome

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**Abstract** **Objective:** To analyze the value of serum creatinine (SCR), cystatin C (CysC) and homocysteine (Hcy) levels

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in predicting the occurrence of contrast-induced nephropathy (CIN) in acute coronary syndrome (ACS) after Percutaneous coronary intervention (PCI). **Methods:** A total of 87 ACS patients admitted to our hospital for PCI from January 2018 to March 2020 were collected continuously. According to whether CIN occurred after the surgery, they were divided into a CIN group (with CIN) and a non-CIN group (without CIN). Serum Scr, CysC and Hcy levels were compared between the 2 groups, and risk factors related to CIN were analyzed by multivariate logistic regression. In addition, ROC curve was drawn to analyze the predictive value of serum CysC and Hcy to CIN. **Results:** A total of 87 patients with ACS were relieved after PCI, but 30 cases developed CIN after PCI, the incidence rate was 34.5%. Smoking, hypertension, and diabetes in the CIN group were significantly higher than those in the non-CIN group (all  $P < 0.05$ ). The serum levels of SCR, CysC and Hcy in the CIN group were significantly higher than those before the operation (all  $P < 0.05$ ), and higher than those in the non-CIN group in the same period (all  $P < 0.05$ ). There was no significant difference in serum SCR, CysC and Hcy between the 2 groups before the operation ( $P > 0.05$ ). Logistic regression analysis showed that serum CysC and Hcy were independent risk factors for CIN. ROC curve showed that the value of serum CysC and Hcy in predicting the occurrence of CIN after 48 h was relatively high, and the optimal critical value of CysC was 1.4 mg/L, AUC was 0.764 (95%CI: 0.664~0.863), while Hcy was 10.2 mol/L, and AUC was 0.813 (95%CI: 0.720~0.907). **Conclusion:** Serum CysC and Hcy are independent influencing factors for CIN complications in ACS patients after PCI, and these indicators are significantly abnormal in these patients. Detection of these indicators 48 h after the surgery can effectively predict the occurrence of CIN.

**Keywords** serum creatinine; cystatin C; homocysteine; acute coronary syndrome; percutaneous coronary intervention; contrast-induced nephropathy

造影剂肾病(contrast-induced nephropathy, CIN)是临床上最常见导致急性肾损伤的原因之一, 具有高发病率和致死率, 且目前尚无特效治疗手段<sup>[1]</sup>。冠脉造影或者急诊经皮冠状动脉介入术(percutaneous coronary intervention, PCI)治疗时往往面临较大的CIN风险<sup>[2]</sup>。因此, 及早且准确地发现CIN并阻止其发展显得极为重要。血清肌酐(serum creatinine, Scr)是目前反映肾功能损伤的常用指标<sup>[3]</sup>。胱抑素C(cystatin C, CysC)又名半胱氨酸蛋白酶抑制剂C, 近年来研究<sup>[4]</sup>发现当肾小球滤过率下降至88 mL/min(正常成人为125 mL/min)时, CysC水平明显升高。血同型半胱氨酸(homocysteine, Hcy)是一项重要的人体健康指标, 当其水平异常升高时, 会大幅增加冠心病、心肌梗死、心力衰竭、动脉粥样硬化的发病风险。最新的研究<sup>[5]</sup>显示: 血Hcy维持在较高水平人群的肾小球滤过率明显下降, 提示血Hcy可导致肾功能减退。因此, 本研究拟分析血清Scr、CysC、Hcy与急性冠脉综合征(acute coronary syndrome, ACS)患者经PCI治疗后CIN发生的关系, 明确上述指标在CIN发病中的作用。

## 1 对象与方法

### 1.1 对象

连续收集2018年1月至2020年3月南京医科大学附属江宁医院收治的择期行PCI治疗的87例ACS患者。纳入标准: 1)符合中华医学会心血管病学学会制定的关于ACS的临床指征描述并经冠状动脉造影确诊<sup>[6]</sup>; 2)符合《中国经皮冠状动脉介入治疗指南(2016)》<sup>[6]</sup>中PCI治疗指征; 3)经南京医科大学附属江宁医院医学伦理委员会批准(伦理号: KY2017-133), 患者知情并签署同意书。排除标准<sup>[7]</sup>: 1)造影剂过敏者; 2)合并凝血功能障碍者; 3)肝肾功能不全或恶性肿瘤者; 4)依从性差, 难以配合完成本研究者。根据患者术后是否发生CIN分为CIN组(发生CIN)与非CIN组(未发生CIN)。其中CIN发生根据欧洲泌尿生殖放射协会(European Society of Urogenital Radiology, ESUR)推荐的CIN判断<sup>[8]</sup>, 将注射造影剂后48~72 h内出现急性肾功能损伤(突发、持续肾功能突然下降), 血清Scr升高绝对值 $\geq 44.2 \mu\text{mol/L}$ 或基线水平升高 $\geq 25\%$ 定义为CIN, 其中基线Scr取入院首测值, 术后Scr取术后不超过72 h测量值。

## 1.2 检测方法

空腹采集外周静脉血5 mL, 避光分离血清, 离心机转速设置为2 500 r/min, 离心半径10 cm, 离心10 min后取上层清液置于灭菌管中, 于-80 °C冰箱保存待测。采用碱性苦味酸终点比色法检测血清Scr, 采用酶联免疫吸附法(enzyme linked immunosorbent assay, ELISA)测定血清CysC, 采用荧光偏振光法检测血清Hcy, 在OlympusAU640全自动生化分析仪(日本协和株式会社提供)进行, Hcy试剂盒购自武汉生之源生物科技有限公司。

## 1.3 统计学处理

采用SPSS 21.0统计学软件进行数据分析, 计数资料以例(%)表示, 2组比较行 $\chi^2$ 检验; 计量资料以均数 $\pm$ 标准差( $\bar{x}\pm s$ )表示, 2组比较行t检验。绘制受试者工作特征(receiver operating characteristic, ROC)曲线分析相关指标对CIN的预测价值。检验水准为 $\alpha=0.05$ ,  $P<0.05$ 为差异有统计学意义。

## 2 结果

### 2.1 PCI术后CIN的发生情况及基线资料比较

87例ACS患者经PCI治疗病情均得到缓解, 术后30例发生CIN, 发生率为34.5%。两组性别、年

龄、体重指数(body mass index, BMI)、既往PCI病史及造影剂用量等基线资料比较, 差异均无统计学意义(均 $P>0.05$ )。CIN组高血压、糖尿病占比均明显高于非CIN组(均 $P<0.05$ , 表1)。

### 2.2 两组手术前后血清Scr、CysC、Hcy水平比较

CIN组术后血清Scr、CysC、Hcy水平明显高于术前水平(均 $P<0.05$ ), 且高于同期非CIN组水平(均 $P<0.05$ )。两组术前血清Scr、CysC、Hcy比较差异均无统计学意义( $P>0.05$ , 表2)。

### 2.3 多因素logistic回归分析

将与CIN发生相关的高血压、糖尿病及血清Scr、CysC、Hcy指标纳入logistic回归模型进行分析, 结果显示血清CysC、Hcy为CIN发生的独立危险因素(表3)。

### 2.4 血清CysC、Hcy水平预测CIN发生的价值分析

选择术后48 h血清CysC、Hcy绘制ROC曲线(图1), 结果显示: 术后48 h血清CysC、Hcy预测CIN发生的价值均较高, 其中CysC预测CIN发生的最佳临界值为1.4 mg/L, AUC为0.764(95%CI: 0.664~0.863), Hcy预测CIN发生的最佳临界值为10.2  $\mu$ mol/L, AUC为0.813(95%CI: 0.720~0.907; 表4)。

表1 两组基线资料比较

Table 1 Comparison of baseline data between the 2 groups

基线资料	CIN组(n=30)	非CIN组(n=57)	$\chi^2/t$	P
年龄/岁	59.1 $\pm$ 8.8	58.0 $\pm$ 9.2	0.538	0.592
性别/[例(%)]			0.036	0.850
男	21 (70.0)	41 (71.9)		
女	9 (30.0)	16 (28.1)		
BMI/(kg·m <sup>-2</sup> )	24.9 $\pm$ 1.2	24.5 $\pm$ 1.0	1.654	0.102
既往史/[例(%)]				
吸烟	12 (40.0)	15 (26.3)	1.720	0.190
饮酒	14 (46.7)	23 (40.4)	0.321	0.571
基础疾病/[例(%)]				
高血压	19 (63.3)	20 (35.1)	6.340	0.011
糖尿病	15 (50.0)	15 (26.3)	4.880	0.027
造影剂用量/mL	174.3 $\pm$ 30.2	166.4 $\pm$ 27.9	1.220	0.226
既往PCI术病史占比/[例(%)]	3 (10.0)	4 (7.0)	0.236	0.627

表2 两组手术前后血清Scr、CysC、Hcy水平比较

Table 2 Comparison of serum Scr, CysC, and Hcy levels between the 2 groups before and after the operation

组别	n	Scr/( $\mu\text{mol}\cdot\text{L}^{-1}$ )	CysC/( $\text{mg}\cdot\text{L}^{-1}$ )	Hcy/( $\mu\text{mol}\cdot\text{L}^{-1}$ )
CIN组	30			
术前		49.4 ± 6.9	0.7 ± 0.2	6.7 ± 1.7
术后		66.7 ± 11.4*#	1.6 ± 0.4*#	12.1 ± 3.0*#
非CIN组	57			
术前		48.4 ± 6.1	0.7 ± 0.1	6.6 ± 1.6
术后		51.8 ± 9.9	0.6 ± 0.4	6.7 ± 1.9

表3 CIN发生的多因素logistic回归分析结果

Table 3 Multivariate logistic regression analysis results of CIN

危险因素	$\beta$	Wald	OR	95%CI	P
高血压	1.245	3.050	3.474	0.859~14.055	0.081
糖尿病	1.333	0.820	3.791	0.212~67.806	0.365
Scr	0.588	6.400	4.424	1.398~14.002	0.061
CysC	1.430	10.597	4.440	1.053~13.862	0.028
Hcy	1.342	0.321	2.348	1.626~4.216	0.009

表4 血清CysC、Hcy水平预测CIN发生的价值分析

Table 4 Analysis of the value of serum CysC and Hcy levels in predicting CIN occurrence

参数	AUC	诊断分界点	敏感性/%	特异性/%	约登指数
术后48 h时CysC水平	0.764	1.4 mg/L	78.5	69.9	0.484
术后48 h时Hcy水平	0.813	10.2 $\mu\text{mol}/\text{L}$	81.4	73.3	0.547

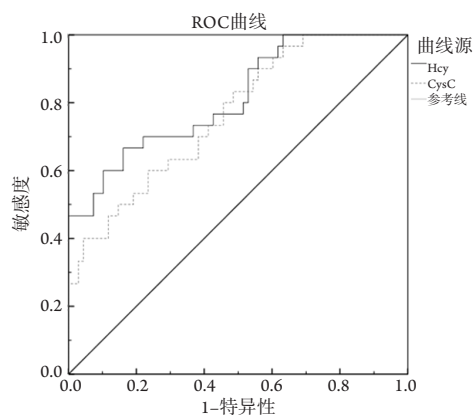


图1 血清CysC、Hcy水平预测CIN发生的ROC曲线

Figure 1 ROC curve of serum CysC and Hcy levels predicting CIN occurrence

### 3 讨论

CIN已经成为院内肾功能衰竭的第三大因素。CIN尚无明确的病理、生理机制,目前主要认为造影剂对肾小管上皮细胞的毒性及造影剂所引起肾血流动力学改变是引起CIN发生的主要原因<sup>[9]</sup>。ACS患者身体机能和各脏器储备功能明显降低,且多合并糖尿病、高血压等,当患者确诊需要行PCI治疗时,较一般老年人群发生CIN的风险更大<sup>[10]</sup>。本研究共收集了87例行PCI治疗的ACS患者,术后30例发展为CIN,发生率为34.5%,提示ACS患者PCI术后CIN发生率高。

临床肾功能评价的最佳指标为肾小球滤过

率, 其估算依赖于血清Scr, 因此临床定义CIN时以血清Scr值升高为诊断标准, 然而临床发现肾脏代偿功能强大, 且血清Scr受年龄、肌肉、种族等多种因素的影响, 只有当肾小球滤过率至少70%损伤时才可能引起Scr值升高<sup>[11-12]</sup>, 提示血肌酐与患者肾小球滤过率的变化并不同步, 导致Scr评估肾小球滤过率并不准确, 通过血清Scr水平诊断CIN有明显滞后性, 并不适用于临床<sup>[13]</sup>。因此寻找更为敏感、高效的指标来预测CIN的发生意义重大, 这已成为当下研究的热点之一。

CysC是一种半胱氨酸蛋白酶抑制剂, 广泛分布于机体的各种体液中, 所有有核细胞都能以稳定的速度生成这种低分子量蛋白质(13 kD), 产生速率恒定, 不受年龄、性别、饮食、代谢等因素影响<sup>[14-15]</sup>。因其分子量小, 电荷中性, 能自由通过肾小球滤过膜, 滤过后由近曲小管完全重吸收和分解, 且不被肾小管分泌, 故CysC是理想的反映肾小球滤过率指标。相关研究<sup>[16]</sup>已肯定了其对肾功能的监测价值。本研究结果显示: CIN患者术后48 h血清CysC水平明显高于术前水平, 且高于同期非CIN患者, logistic回归模型结果显示CysC是CIN发生的独立危险因素。ROC曲线显示术后48 h血清CysC水平诊断CIN的AUC为0.764, 且敏感度、特异度相对较高, 提示CysC相较于传统血清Scr等指标, 对CIN的早期预测价值更高。

Hcy是一种含巯基的氨基酸, 在血浆中80%~90%与蛋白结合而存在, 其水平与肾损伤存在一定的相关性<sup>[17]</sup>。目前研究<sup>[18]</sup>结果显示: Hcy在肾损伤中可能包含的潜在机制有氧化应激、炎症、内质网激活、内皮损伤等。为进一步了解ACS患者PCI术后发生CIN的相关性, 本研究通过多因素logistic分析发现Hcy为术后CIN发生的独立危险因素, 这说明高同型半胱氨酸血症可能本身对CIN的发生有一定影响, 同时提示肾功能下降, Hcy的清除减少, 肾功能也将对CIN的发生产生影响。本研究绘制ROC曲线发现血清Hcy预测CIN发生价值较高, 当术后48 h Hcy超过10.2  $\mu\text{mol/L}$ 时高度怀疑发生CIN。

综上所述, 血清CysC、Hcy为ACS患者PCI术后并发CIN的独立影响因素, 该类患者体内上述指标水平明显异常, 术后48 h对上述指标进行检测可有效预测CIN发生。后续仍需进行更加深入的研究, 以明确血清CysC、Hcy在ACS患者PCI术后并发CIN中的具体作用机制。

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