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急性冠脉综合征患者血清胱抑素C水平与冠脉病变程度的关系

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摘　要

目的：探讨血清胱抑素C水平(CysC)与急性冠脉综合征(Acute coronary syndrome, ACS)患者冠脉病变程度的关系。方法：选取经冠状动脉造影检查确诊ACS的253例患者作为观察组，40例同期经冠脉造影检查排除冠心病的患者作为对照组。入院后检测患者次日晨起空腹血清胱抑素C水平，将ACS患者血清CysC水平与Gensini评分作相关性分析。结果：随着冠脉病变程度的增加，血清CysC、尿酸(UA)水平逐渐升高，组间比较差异均有统计学意义($P < 0.01$)。血清CysC、UA水平与ACS患者Gensini评分呈正相关($P < 0.05$)，是影响Gensini评分的危险因素($P < 0.05$)。结论：ACS患者血清CysC、UA水平与冠脉病变严重程度相关，是使冠脉病变程度加重的危险因素。对ACS患者进行监测和早期干预治疗，有助于预防心血管不良事件的发生。

关键词

急性冠脉综合征，胱抑素C，尿酸，Gensini评分

Association of Serum Cystatin C Levels with Disease Severity in Patients with Acute Coronary Syndrome

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Abstract

Objective: To investigate the correlation between coronary artery lesion score and serum cystatin C (CysC) level in acute coronary syndrome (ACS). Methods: 253 patients were admitted from January 2019 to December 2019 with ACS and 39 patients without ACS (the control group) were enrolled in the study. All subjects underwent coronary angiography. ACS patients were divided into the low score group, the middle score group and the high score group by coronary artery stenosis score (Gensini); patients in the control group were excluded with coronary artery disease by coronary angiography. Serum CysC levels were measured within 24 h after admission. The correlation between CysC level and Gensini score was compared. Results: With the increase of severity of coronary artery disease, the levels of CysC and uric acid (UA) were increased. The difference between groups was highly statistically significant ($P < 0.01$). Logistic regression analysis showed that Gensini scores were positively correlated with levels of CysC and UA ($P < 0.05$). High serum CysC and UA levels were independent risk factors for high Gensini scores. Conclusion: The levels of serum CysC and UA in ACS patients are related to the severity of coronary artery lesion, and are the risk factors of the severity of coronary artery lesion. In clinical work, monitoring of the above indicators and early intervention therapy for ACS patients were of great clinical significance for preventing the occurrence of acute coronary events.

Keywords

Acute Coronary Syndrome, Cystatin C, Uric Acid, Gensini Scores

1. 引言

急性冠脉综合征(Acute coronary syndrome, ACS)是影响及危害人类健康的疾病之一，是导致死亡和残疾的主要原因[1] [2]。ACS 病理生理机制复杂，其中炎症起着重要作用。炎性标志物水平的升高与心血管不良事件发生率密切相关。胱抑素 C (cystatin C, CysC)是半胱氨酸蛋白酶抑制剂蛋白 C 的简称，由于其分子量小，每日分泌量恒定，并且可由肾小球滤过并被肾小管重吸收，与性别、年龄、和肌肉质量无关，同时参与多种炎症反应[3] [4] [5] [6]。缺氧条件下，心肌细胞产生 CysC 并将其释放到血液中[7]。众多研究表明[8] [9] [10]，血清 Cys C 水平与炎症、无症状性心力衰竭及动脉粥样硬化斑块的发生发展有关。这些特性可能使 Cys C 成为 ACS 早期诊断、病情评估的潜在生物标志物。胱抑素 C 水平变化预示心血管系统斑块负荷变化，故对 ACS 患者血清 CysC 变化与冠脉病变程度的关系进行了研究。

2. 资料与方法

2.1. 一般资料

选取对象为 2019 年 1 月~12 月就诊于青岛大学附属医院确诊为 ACS 并接受冠脉造影的患者 253 例作为观察组，根据 Gensini 评分将 ACS 患者分为低分组 86 例、中分组 85 例、高分组 82 例。选取同期经

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冠脉造影检查排除冠心病的患者 40 例作为对照组。纳入对象标准：符合 ACS 诊断标准并在住院期间行冠脉造影患者。参照美国心脏病协会急性冠脉综合征患者诊断和管理指南标准[11] [12] [13]。排除标准：1) 严重感染或自身免疫疾病患者；2) 先天性心脏病、大血管疾病、血管畸形；3) 严重肝肾功不全；4) 合并慢性消耗性疾病；5) 既往心肌梗死病史、冠状动脉支架植入术或冠状动脉搭桥术。

2.2. 方法

所有患者均根据患者病历记录性别、年龄、高血压病史、糖尿病史，患者次日早晨禁食、禁水 8~10 小时后抽取静脉血送检验科检测肾功能。

2.2.1. 冠状动脉病变评分方法

采用美国心脏病学会推荐的 Gensini 积分系统[14]对冠状动脉狭窄程度评估积分：≤25%狭窄计 1 分；26%~49%狭窄计 2 分；50%~74% 狭窄计 4 分；75%~89%狭窄计 8 分；90%~99%狭窄计 16 分；100%狭窄计 32 分。病变分支记分：左主干病变为 5 分，左前降支或回旋支近段为 2.5 分，左前降支中段为 1.5 分，左前降支远段为 1.0 分，左回旋支中、远段为 1 分，右冠状动脉近、中、远段为 1 分，小分支为 0.5 分，Gensini 评分 = Σ (冠脉狭窄程度 × 病变部位系数)，得分越高说明患者病情越严重，0~17 分为轻度病变，18~44 分为中度病变，>44 分为重度病变。

2.2.2. 统计方法

采用 SPSS 23.0 软件对所得数据进行分析，定量资料采用均数±标准差表示，用 t 检验比较两组均数，多组间比较满足正态分布的计量资料采用方差分析，不满足正态分布的计量资料采用秩和检验；定性资料用百分比表示，采用 χ^2 检验。相关性分析时若满足正态分布用 Pearson 相关性分析，不满足正态分布则用 *Spearman* 相关性分析。采用逐步向前法建立多因素 *logistic* 回归模型。当结局变量为二分类时建立非条件 *logistic* 回归模型，当结局变量为有序分类变量时，建立有序 *logistic* 回归模型，以 *P* < 0.05 为差异有统计学意义。

3. 结果

1) 基线资料比较 ACS 组和对照组在性别构成、CysC、Cr、UA、Gensini 评分及合并高血压差异有统计学意义(*P* < 0.05)，而年龄及合并糖尿病差异无统计学(*P* > 0.05)。见表 1。

Table 1. Clinical data of ACS group and control group were compared
表 1. ACS 组与对照组临床资料比较($\bar{x} \pm s$)

项目	对照组(n = 40)	ACS 组(n = 253)	t/χ^2	*P*
年龄(岁)	57.88 ± 7.96	60.68 ± 9.33	−1.796	0.073
性别(男性/女性)	13/27	174/79	19.684	0.000
CysC (mg/L)	0.78 ± 0.12	0.93 ± 0.20	−4.295	0.000
Cr (umol/L)	53.35 ± 14.26	65.35 ± 16.64	−4.313	0.000
UA (umol/L)	310.70 ± 79.31	351.12 ± 86.95	−2.764	0.006
Gensini 评分	1.30 ± 8.22	38.79 ± 2.18	−6.639	0.000
糖尿病史(n, %)	5 (1.7)	50 (17.1)	1.195	0.274
高血压病史(n, %)	15 (5.1)	147 (50.2)	5.931	0.015

注：BMI：体重指数；Cr：肌酐；UA：尿酸。

2) ACS 组不同 Gensini 评分组间指标比较随着病变程度增加，CysC、UA 水平逐渐升高，差异有统计学意义($P < 0.05$)；而性别构成、Cr 合并高血压无统计学差异($P > 0.05$)。见表 2。

Table 2. Comparison of clinical data between different Gensini ratings in ACS group
表 2. ACS 组不同 Gensini 评分组间临床资料的比较($\bar{x} \pm s$)

项目	低分组(n = 86)	中分组(n = 85)	高分组(n = 82)	χ^2/F	P
性别(男性/女性)	53/33	57/28	64/18	5.446	0.066
CysC (mg/L)	0.83 ± 0.11	0.91 ± 0.14[①]	1.05 ± 0.26[①②]	31.628	0.000
Cr (umol/L)	62.48 ± 19.24	65.40 ± 14.45	68.25 ± 15.46	2.550	0.080
UA (umol/L)	319.49 ± 79.97	350.63 ± 95.13[①]	384.80 ± 72.21[①②]	12.965	0.000
高血压病史(n, %)	49 (19.4)	46 (18.2)	52 (20.6)	1.550	0.461

注：[①]与低分组比较，$P < 0.05$；[②]与中分组比较，$P < 0.05$。

3) CysC、UA 与 ACS 组不同 Gensini 评分组之间相关性 CysC、UA 与不同 Gensini 评分组均成正相关，相关系数分别为 0.449、0.307，P 均为 0.00。

4) ACS 组 Gensini 积分与其他因素多变量 *Logistic* 回归分析以 Gensini 评分为因变量，CysC、UA 为自变量完全进入多变量回归分析，结果显示，CysC、UA 是影响 Gensini 评分的独立危险因素($P < 0.05$)。见表 3。

Table 3. Multivariate *Logistic* regression analysis of Gensini score and other factors
表 3. Gensini 评分与其他因素多变量 *Logistic* 回归分析

因素	OR	95%CI	P
CysC	10.353	6.920~13.786	0.00
UA	9.026	5.588~12.464	0.00

4. 讨论

急性冠脉综合征(ACS)是指冠状动脉内不稳定的粥样硬化斑块破裂或糜烂继发新鲜血栓形成所导致的心脏急性缺血综合征。ACS 在我国发病率依然呈逐年增加的态势[15]。ACS 患者由于动脉粥样硬化斑块破裂，进而引起止血反应，从而导致梗死。因 ACS 发病急、进展快、病死率高，早期进行危险评估和积极干预具有重要意义。炎性标志物支持的心血管疾病风险评估是对高危人群进行分层和优化患者治疗的首要要求[16]。

近期，有研究显示，胱抑素 C 不仅能反应肾小球滤过功能、预期早期损伤，CysC 也已经成为心血管风险的潜在标记[17]。CysC 是肾功能的血清标志物，有研究表明，肾小球滤过率仍在正常范围内时，心血管疾的风险已经开始升高。CysC 血清浓度似乎与个体因素无关[18]。在心血管事件发生发展的不同阶段，胱抑素 C 水平可能会出现不同变化状态，提示其在心血管疾病的发展过程中的分泌、消耗、激活状态的转变。在动脉粥样硬化的发生发展过程中，CysC 水平增高，提示半胱氨酸蛋白酶过度激活，细胞外基质降解引起体内炎症因子激活，诱发内皮损伤及功能障碍，循环凝血与纤溶系统失衡，微血管重构，引起微循环血管阻力增高及血栓形成。在此背景下，CysC 也被认为是有症状的冠心病和糖尿病患者死亡和心血管事件的一个更强的预测因子[19] [20]。本研究中，与对照组相比，ACS 患者血清 CysC 水平显著升高。此外，冠状动脉狭窄程度与血清中 CysC 表达水平有关。多因素 *logistic* 回归分析显示，血清 CysC

浓度升高可能是 ACS 的影响因素，也可能是冠脉狭窄程度的危险因素。因此，测定血清 CysC 水平对鉴别 ACS 高危人群和预测 ACS 的严重程度有重要意义。高 CysC 水平是 ACS 的危险因素，对心血管不良事件的早期诊断和预防有重要作用[21]。结果证实 CysC 在急性冠脉综合征诊断中具有早期预测价值[22][23]。众多研究表明，血清尿酸水平与动脉粥样硬化的相关指标(如炎症标志物，氧化应激和内皮功能障碍)之间存在显著关系。尿酸水平的升高可以提示血管内皮存在功能障碍。高尿酸血症与血管内皮细胞中一氧化氮生成减少之间具有相关性。内皮衍生的一氧化氮是冠状动脉血流的重要调节剂，具有强烈的血管舒张作用。

此外，本研究有一些局限性。首先，本研究结果仅提示 CysC 与 ACS 之间存在相关性。由于样本量有限，没有进一步探讨血清 CysC 水平与不同 ACS 类型之间的关系。其次，本研究就没有探讨血清 CysC 水平与冠脉病变支数之间的关系；最后，这是一项单中心研究，涉及的患者相对较少，存在一定的局限及不足，搜集数据较少、测定相关检验检查项目较少、抽样存在偏倚等均对研究统计有一定负面影响。

5. 结论

高血清 CysC、UA 水平与 ACS 患者狭窄冠状动脉程度是独立相关的。因此，血清 CysC 可能是 ACS 潜在的标志物。血清 CysC 水平可能对鉴别 ACS 高危人群、预测患者狭窄程度、预防心血管不良事件有一定的参考价值。

声　明

该研究已获得相应伦理许可。

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