

血清同型半胱氨酸水平对急性冠脉综合征患者的影响及其与冠状动脉病变支数、冠状动脉病变严重程度的相关性研究

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【摘要】 目的 探讨血清同型半胱氨酸 (Hcy) 水平对急性冠脉综合征 (ACS) 患者的影响及其与冠状动脉病变支数、冠状动脉病变严重程度的相关性。**方法** 选择 2013—2015 年安徽医科大学附属合肥医院收治的 ACS 患者 84 例, 根据血清 Hcy 水平分为 Hcy 正常组 (对照组, $n = 36$) 和 Hcy 升高组 (研究组, $n = 48$)。比较两组患者的一般资料 [年龄、性别、ACS 分型、合并疾病 (高血压、高脂血症、糖尿病)、既往史 (冠心病家族史、吸烟史、心肌梗死病史、冠状动脉支架置入术史及冠状动脉旁路移植术史)]、实验室检查指标 [随机血糖、心肌肌钙蛋白 I (cTnI)、肌酸激酶同工酶 (CK-MB)、空腹血糖、总胆固醇 (TC)、低密度脂蛋白胆固醇 (LDL-C)、三酰甘油 (TG)、超敏 C 反应蛋白 (hs-CRP)]、冠状动脉病变支数及 SYNTAX 评分, 血清 Hcy 水平与冠状动脉病变支数、SYNTAX 评分的相关性分析采用 Spearman 秩相关性分析。**结果** 两组患者年龄、性别、高血压发生率及冠心病家族史、心肌梗死病史、冠状动脉支架置入术史阳性率比较, 差异无统计学意义 ($P > 0.05$); 研究组患者 ACS 分型差于对照组, 高脂血症、糖尿病发生率及吸烟史阳性率高于对照组 ($P < 0.05$), 两组患者中无一例有冠状动脉旁路移植术史。研究组患者随机血糖、cTnI、CK-MB、空腹血糖、TC、LDL-C、TG、hs-CRP 及 SYNTAX 评分高于对照组, 冠状动脉病变支数多于对照组 ($P < 0.05$)。Spearman 秩相关性分析结果显示, 血清 Hcy 水平与 ACS 患者冠状动脉病变支数 ($r_s = 0.238, P < 0.05$)、SYNTAX 评分呈正相关 ($r_s = 0.870, P < 0.05$)。**结论** Hcy 水平升高的 ACS 患者血糖、血脂水平更高, 心功能损伤和冠状动脉病变程度更严重, 且血清 Hcy 水平与冠状动脉病变支数、冠状动脉病变程度有关。

【关键词】 急性冠脉综合征; 半胱氨酸; 冠状动脉疾病; SYNTAX 评分

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Impact of Serum Homocysteine Level on Patients with Acute Coronary Syndrome and Its Correlations with Number of Stenosed Coronary Arteries and SYNTAX Score HAN Yu-long, LIANG Li-long, XU Ming-sheng, ZHANG Jian, YANG Lin-fei. Department of Cardiology, Hefei Hospital Affiliated to Anhui Medical University (the Second People's Hospital of Hefei), Hefei 230011, China

【Abstract】 **Objective** To investigate the impact of serum homocysteine level on patients with acute coronary syndrome and its correlations with number of stenosed coronary arteries and SYNTAX score. **Methods** A total of 84 patients with acute coronary syndrome were selected in Hefei Hospital Affiliated to Anhui Medical University from 2013 to 2015, and they were divided into control group (with normal serum homocysteine level, $n = 36$) and study group (with elevated serum homocysteine level, $n = 48$) according to the serum homocysteine level. General information [including age, gender, types of acute coronary syndrome, complications (such as hypertension, hyperlipidaemia and diabetes), past medical history (such as family history of coronary heart disease, smoking history, history of myocardial infarction, coronary stent implantation history and coronary artery bypass grafting history)], laboratory examination results [including random plasma glucose (RPG), cTnI, CK-MB, fasting plasma glucose (FPG), TC, LDL-C, TG and hs-CRP), number of stenosed coronary arteries and SYNTAX score were compared between the two groups, correlations between serum homocysteine level and number of stenosed coronary arteries, and

SYNTAX score were analyzed by Spearman correlation analysis. **Results** No statistically significant differences of age, gender, incidence of hypertension, positive rate of family history of coronary heart disease, history of myocardial infarction or coronary stent implantation history was found between the two groups ($P > 0.05$); the proportion of STEMI, incidence of hyperlipidaemia and diabetes, and positive rate of smoking history of study group were statistically significantly higher than those of control group ($P < 0.05$); no one of the two groups received coronary artery bypass grafting. RPG, cTnI, CK-MB, FPG, TC, LDL-C, TG, hs-CRP and SYNTAX score of study group were statistically significantly higher than those of control group, and number of stenosed coronary arteries of study group was statistically significantly more than that of control group ($P < 0.05$). Spearman correlation analysis results showed that, serum homocysteine level was positively correlated with number of stenosed coronary arteries ($r_s = 0.238$, $P < 0.05$) and SYNTAX score, respectively ($r_s = 0.870$, $P < 0.05$). **Conclusion** The levels of blood glucose and blood lipid of acute coronary syndrome patients with elevated serum homocysteine level are higher, heart function injury and the severity of coronary artery disease are more severe, meanwhile serum homocysteine level is correlated with the number of stenosed coronary arteries and severity of coronary artery disease, respectively.

【Key words】 Acute coronary syndrome; Cysteine; Coronary artery disease; SYNTAX score

近年来,急性冠脉综合征(acute coronary syndrome, ACS)发病率逐年升高,其具有发病急、病情重且进展快等特点,病死率较高,因此对 ACS 患者进行早期预防、危险评估和积极干预尤为重要。冠心病的传统危险因素包括高血压、糖尿病、血脂异常、肥胖及吸烟等,但针对危险因素采取措施后临床控制效果和患者预后仍不甚理想。近年来,有多项研究指出,高同型半胱氨酸血症是冠心病的独立危险因素^[1-6]。血清同型半胱氨酸(Hcy)水平是 ACS 患者死亡的预测因子之一,血清 Hcy 水平升高可导致 ACS 患者血管内皮功能紊乱,进而加重冠状动脉粥样硬化及引发缺血性心脑血管事件^[7]。有研究显示,血清 Hcy 水平下降并未降低 ACS 患者心血管疾病再发风险^[8-11],故血清 Hcy 水平与 ACS 的相关性及其能否作为危险评估指标还需进一步研究。本研究旨在探讨血清 Hcy 水平对 ACS 患者的影响及其与冠状动脉病变支数、冠状动脉病变严重程度的相关性,现报道如下。

1 对象与方法

1.1 诊断标准 ACS 包括急性心肌梗死(AMI)和不稳定型心绞痛(UAP)。AMI 诊断标准:(1)具有缺血性胸痛史;(2)心电图出现动态演变;(3)血清心肌标志物水平出现动态改变。具备上述 2 或 3 条标准即可诊断为 AMI。UAP 诊断标准:(1)近 2 个月内新发心绞痛;(2)心绞痛在休息或安静状态下发生;(3)胸痛程度加重、发作次数增加、持续时间延长,且诱发心绞痛的活动阈值明显减低;(4)心绞痛发生在 AMI 发病后 24 h~1 个月内;(5)胸痛发作时心电图检查显示 ST 段一过性抬高,心绞痛发作时心电图显示 ST 段压低 ≥ 0.1 mV 或相连 2 个及以上导联 T 波倒置,也可表现为正常,但心肌肌钙蛋白 I(cTnI)和肌酸激酶同工酶(CK-MB)水平在参考范围。

1.2 纳入与排除标准 纳入标准:(1)符合 ACS 的诊

断标准;(2)经冠状动脉造影检查证实冠状动脉主血管(左主干、左前降支、左回旋支及右冠状动脉)中的任意一支狭窄率 $\geq 50\%$ 。排除标准:(1)合并急性肝、肾功能不全患者;(2)妊娠期妇女及近期应用叶酸制剂、避孕药、维生素 B₆ 和维生素 B₁₂ 等影响 Hcy 代谢药物患者;(3)合并免疫系统疾病、恶性肿瘤、甲状腺功能异常患者;(4)合并营养不良及巨幼红细胞性贫血患者。

1.3 研究对象 选择 2013—2015 年安徽医科大学附属合肥医院收治的 ACS 患者 84 例,均经冠状动脉造影检查确诊并行经皮冠状动脉介入治疗。所有患者中男 51 例,女 33 例;平均年龄(61.4 \pm 12.6)岁;UAP 40 例,ST 段抬高型心肌梗死(ST segment elevation myocardial infarction, STEMI) 32 例,非 ST 段抬高型心肌梗死(non ST segment elevation myocardial infarction, NSTEMI) 12 例。血清 Hcy 水平参考范围为 5~15 $\mu\text{mol/L}$,根据血清 Hcy 水平将所有患者分为 Hcy 正常组(对照组, $n = 36$)和 Hcy 升高组(研究组, $n = 48$)。

1.4 资料收集 (1)比较两组患者一般资料,包括年龄、性别、ACS 分型(UAP、STEMI、NSTEMI)、合并疾病(高血压、高脂血症、糖尿病)、既往史(冠心病家族史、吸烟史、心肌梗死病史、冠状动脉支架置入术史及冠状动脉旁路移植术史)等。(2)入院时抽取患者静脉血检测随机血糖、cTnI、CK-MB;次日晨起再次抽取患者静脉血检测空腹血糖及总胆固醇(TC)、低密度脂蛋白胆固醇(LDL-C)、三酰甘油(TG)、超敏 C 反应蛋白(hs-CRP)。

1.5 治疗方法 患者入院后均按照 ACS 诊疗指南给予阿司匹林、氯吡格雷、血管紧张素转换酶抑制剂(ACEI)、美托洛尔、他汀类药物及低分子肝素治疗。STEMI 患者需在发病 12 h 内行急诊冠状动脉造影、血栓抽吸、球囊扩张术或冠状动脉支架置入术;而 UAP、

NSTEMI 患者则根据危险分层分别给予急诊、择期（入院 10 d 内）冠状动脉造影 + 经皮冠状动脉介入治疗，以冠状动脉内无残余狭窄、TIMI 血流 3 级为手术成功。根据冠状动脉优势型、冠状动脉病变数、病变节段数及权重结合其病变特征应用 2.11 版网络计算器计算 SYNTAX 评分^[12]，并分析 ACS 患者血清 Hcy 水平与冠状动脉病变支数、SYNTAX 评分的相关性。冠状动脉造影结果由 2 位高年资介入医师经桡动脉进行判读，并以国际通用的直径法评估造影结果，即冠状动脉狭窄率 ≥ 50% 作为有意义的病变，左主干狭窄率 ≥ 50% 而无前降支或回旋支病变为单支病变。

1.6 统计学方法 采用 SPSS 19.0 统计学软件进行数据分析，计量资料以 $(\bar{x} \pm s)$ 表示，采用 *t* 检验；计数资料以相对数表示，采用 χ^2 检验；血清 Hcy 水平与冠状动脉病变支数、SYNTAX 评分的相关性分析采用 Spearman 秩相关性分析。以 *P* < 0.05 为差异有统计学意义。

2 结果

2.1 一般资料 两组患者年龄、性别、高血压发生率及冠心病家族史、心肌梗死病史、冠状动脉支架置入史阳性率比较，差异无统计学意义 (*P* > 0.05)；研究组患者 STEMI 所占比例，高脂血症、糖尿病发生率及吸烟史阳性率高于对照组，差异有统计学意义 (*P* < 0.05，见表 1)；两组患者中无一例有冠状动脉旁路移植术史。

2.2 实验室检查指标、冠状动脉病变支数及 SYNTAX

评分 研究组患者随机血糖、cTnI、CK-MB、空腹血糖、TC、LDL-C、TG、hs-CRP 及 SYNTAX 评分高于对照组，冠状动脉病变支数多于对照组，差异有统计学意义 (*P* < 0.05，见表 2)。

2.3 相关性分析 Spearman 秩相关性分析结果显示，血清 Hcy 水平与 ACS 患者冠状动脉病变支数 (*r*_s = 0.238, *P* < 0.05)、SYNTAX 评分呈正相关 (*r*_s = 0.870, *P* < 0.05)。

3 讨论

ACS 包括 UAP 和 AMI，是由于冠状动脉内易损斑块破裂、血小板聚集、血栓形成继发冠状动脉不完全或完全阻塞所致的一组临床综合征，其发病急、病情重，常危及患者生命安全，因此加强临床基础研究、尽早识别并积极干预对改善 ACS 患者预后意义重大。近年来，有研究发现，血清 Hcy 水平可作为反映冠状动脉病变程度的临床指标，但也有研究得出不一致的结论。本研究旨在探讨血清 Hcy 水平对 ACS 患者的影响及其与冠状动脉病变支数、冠状动脉病变严重程度的相关性。

Hcy 是由蛋氨酸去甲基化形成的一种含硫氨基酸。临床研究表明，血清 Hcy 水平升高可能会导致机体血管内皮细胞功能障碍，而内源性一氧化氮 (NO) 生成减少是导致血管内皮细胞功能障碍的主要机制。血清 Hcy 水平升高会增加不对称二甲基精氨酸 (ADMA) 分泌，进而导致内皮型一氧化氮合酶 (eNOS) 解耦联，继发 NO 合成减少及超氧化物歧化酶合成增加^[13-14]，从而影响血管内皮功能。此外，高水平 Hcy 可能通过诱发氧化

表 1 两组患者一般资料比较

Table 1 Comparison of general information between the two groups

组别	例数	年龄 ($\bar{x} \pm s$, 岁)	性别 (男/女)	ACS 分型[n(%)]			高血压 [n(%)]	高脂血症 [n(%)]	糖尿病 [n(%)]	冠心病 家族史 [n(%)]	吸烟史 [n(%)]	心肌梗 死病史 [n(%)]	冠状动脉支 架置入术史 [n(%)]
				UAP	STEMI	NSTEMI							
对照组	36	63.4 ± 10.6	25/11	18(50.0)	12(33.3)	6(16.7)	22(61.11)	9(25.00)	6(16.67)	4(11.11)	17(47.22)	3(8.33)	4(11.11)
研究组	48	59.8 ± 13.6	34/14	22(45.8)	20(41.7)	6(12.5)	31(64.58)	17(35.42)	14(29.12)	6(12.50)	31(64.58)	5(10.42)	6(12.50)
$\chi^2(t)$ 值		0.93 ^a	1.21		5.74		1.16	6.61	9.42	0.25	4.58	1.38	1.25
<i>P</i> 值		0.250	0.070		0.032		0.340	0.002	<0.001	0.270	0.020	0.080	0.470

注：^a 为 *t* 值；ACS = 急性冠脉综合征，UAP = 不稳定型心绞痛，STEMI = ST 段抬高型心肌梗死，NSTEMI = 非 ST 段抬高型心肌梗死

表 2 两组患者实验室检查指标、冠状动脉病变支数及 SYNTAX 评分比较

Table 2 Comparison of laboratory examination results, number of stenosed coronary arteries and SYNTAX score between the two groups

组别	例数	随机血糖 ($\bar{x} \pm s$, mmol/L)	cTnI ($\bar{x} \pm s$, mg/L)	CK-MB ($\bar{x} \pm s$, U/L)	空腹血糖 ($\bar{x} \pm s$, mmol/L)	TC ($\bar{x} \pm s$, mmol/L)	LDL-C ($\bar{x} \pm s$, mmol/L)	TG ($\bar{x} \pm s$, mmol/L)	hs-CRP ($\bar{x} \pm s$, mg/L)	冠状动脉病变支数[n(%)]				SYNTAX 评 分($\bar{x} \pm s$, 分)
										单支	双支	三支	多支	
对照组	36	6.64 ± 1.12	6.68 ± 4.25	74.14 ± 68.93	5.26 ± 0.70	2.96 ± 1.20	2.26 ± 0.84	1.39 ± 0.64	5.44 ± 3.42	19(52.78)	11(30.56)	4(12.50)	2(5.56)	16.3 ± 8.2
研究组	48	9.12 ± 1.84	9.36 ± 5.28	112.66 ± 97.72	7.86 ± 1.76	5.06 ± 1.24	4.38 ± 0.89	2.68 ± 0.90	9.28 ± 5.32	22(45.83)	14(29.17)	8(16.67)	4(8.33)	28.4 ± 9.1
<i>t</i> (χ^2)值		5.82	3.36	3.57	5.51	3.85	6.03	4.79	3.96		4.92 ^a			9.56
<i>P</i> 值		<0.001	0.032	0.026	<0.001	0.002	<0.001	0.001	0.004		0.031			<0.001

注：^a 为 χ^2 值；cTnI = 心肌肌钙蛋白 I，CK-MB = 肌酸激酶同工酶，TC = 总胆固醇，LDL-C = 低密度脂蛋白胆固醇，TG = 三酰甘油，hs-CRP = 超敏 C 反应蛋白

应激反应而导致机体产生氧自由基及过氧化物, 进而引发血管内皮功能损伤; 高水平 Hcy 还可使前列腺素、缓激肽等抗炎性细胞因子减少及甲基化, 引发血管内皮功能障碍^[15-22], 导致动脉粥样硬化的发生发展。MONTALESCOT 等^[23] 研究结果显示, 冠心病患者血清 Hcy 水平越高则患者冠状动脉病变越严重, 病变支数及病变部位越多。血清 Hcy 水平升高是心脑血管疾病及外周动脉粥样硬化的独立危险因素, 且其与冠状动脉病变严重程度及预后不良相关^[24-28]。本研究结果显示, 研究组患者高脂血症、糖尿病发生率、吸烟史阳性率及随机血糖、cTnI、CK-MB、空腹血糖、TC、LDL-C、TG、hs-CRP 高于对照组, 提示血清 Hcy 水平升高的 ACS 患者血糖、血脂水平更高, 心功能损伤更严重。

冠状动脉病变严重程度评分系统常具有一定主观性, 故常导致研究结果发生差异。本研究采用 SYNTAX 评分系统评估 ACS 患者冠状动脉病变严重程度, 该评分系统是根据冠状动脉病变解剖特点进行危险分层的一种新的评分系统, 可根据冠状动脉病变位置、严重程度、分叉、钙化等解剖特点定量评价冠状动脉病变复杂程度, 已成为目前评估 ACS 患者冠状动脉病变严重程度的有效评分系统之一。本研究结果显示, 研究组患者 ACS 分型差于对照组、冠状动脉病变支数多于对照组、SYNTAX 评分高于对照组, 且 Spearman 秩相关性分析结果显示, 血清 Hcy 水平与 ACS 患者冠状动脉病变支数、SYNTAX 评分呈正相关, 提示血清 Hcy 水平升高与冠状动脉病变严重程度有关, 故检测血清 Hcy 水平对 ACS 的危险评估具有重要的临床意义, 与 MONTALESCOT 等^[23] 研究结果一致。

综上所述, Hcy 水平升高的 ACS 患者血糖、血脂水平更高, 心功能损伤和冠状动脉病变程度更严重, 且血清 Hcy 水平与冠状动脉病变支数、冠状动脉病变程度有关。但本研究为单中心研究、样本量较小、缺乏长期随访、未观察血清 Hcy 水平与心血管疾病预后及不良事件的相关性, 且血清 Hcy 水平与冠心病的病因学关系及其导致冠状动脉粥样硬化病变的确切发病机制目前尚不明确, 血清 Hcy 水平能否作为 ACS 的治疗靶点及其与患者预后的关系尚需大样本量的前瞻性研究进一步证实。

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