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缺血性心肌病患者血清 D-二聚体、同型半胱氨酸与左室重构 相关参数的相关性

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[摘要] 目的: 探讨缺血性心肌病(ischemic cardiomyopathy, ICM)患者血清D-二聚体(D-dimer, DD)、同型半胱氨酸(homocysteine, HCY)与左室重构的关系, 旨在为ICM左室重构的早期诊断提供参考。方法: 选择2016年6月至2019年6月成都市龙泉驿区第一人民医院收治的130例ICM患者为研究对象, 依据冠状动脉造影结果将ICM患者分为重构组(左室重构, $n=95$)和无重构组(无左室重构, $n=35$), 比较ICM不同心功能分级患者血清DD和HCY水平, 左室重构参数[左室舒张末期内径(left ventricular end-diastolic diameter, LVEDd), 左室后壁厚度(left ventricular posterior wall thickness, LVPW), 左室射血分数(left ventricular ejection fraction, LVEF)]。采用单因素、二元logistic回归分析ICM患者左室重构的影响因素, Pearson参数分析ICM患者血清DD和HCY水平与左室重构的相关性。结果: ICM患者心功能分级越高, 血清DD和HCY水平越高, 差异有统计学意义($P<0.05$); ICM患者心功能分级越高, LVEDd和LVPW越厚而LVEF越低。不同心功能分级患者LVEDd, LVPW和LVEF两两比较, 差异有统计学意义($P<0.05$)。血清DD(OR=1.102, 95%CI: 1.016~1.382), HCY(OR=1.685, 95%CI: 1.009~2.798)水平是ICM患者左室重构的危险因素($P<0.05$)。ICM患者血清DD、HCY水平与LVEDd、LVPW呈明显正相关, 而与LVEF呈明显负相关($r=0.502, 0.518, -0.673; r=0.643, 0.592, -0.687, P<0.05$)。结论: ICM患者血清DD和HCY水平明显升高, LVEDd和LVPW显著增大而LVEF明显降低, 且ICM患者血清DD和HCY水平与左室重构参数呈明显相关性, DD和HCY水平与ICM病情程度密切相关。

[关键词] 缺血性心肌病; D-二聚体; 同型半胱氨酸; 左室重构

Correlation between serum D-dimer, homocysteine and left ventricular remodeling parameters in patients with ischemic cardiomyopathy

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Abstract **Objective:** To explore the relationship between serum D-dimer (DD), homocysteine (HCY) and left ventricular

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remodeling in patients with ischemic cardiomyopathy (ICM), aiming to provide reference for early diagnosis of ICM left ventricular remodeling. **Methods:** One hundred and thirty patients with ICM who were admitted and treated at the hospital between June 2016 and June 2019 were selected as subjects. According to the results of coronary angiography, subjects were divided into a remodeling group (left ventricular remodeling, $n=95$) and a non-remodeling group (no left ventricular remodeling, $n=35$). The levels of serum DD and HCY, and left ventricular remodeling parameters [left ventricular end-diastolic diameter (LVEDd), left ventricular posterior wall thickness (LVPW), left ventricular ejection fraction (LVEF)] were compared between patients with different grades of cardiac function. Univariate and binary regression analyses were performed to analyze influencing factors of left ventricular remodeling in patients with ICM. Pearson parameters were used to analyze the correlation between serum DD, HCY levels and left ventricular remodeling in patients with ICM. **Results:** For patients with ICM, the higher the cardiac function grading, the higher serum DD and HCY levels. The difference was statistically significant ($P<0.05$); the higher the cardiac function grading, the larger LVEDd and LVPW, and the lower LVEF. Differences in LVEDd, LVPW and LVEF of patients with different grades of cardiac function were statistically significant ($P<0.05$). Serum DD [odds ratio (OR)=1.102, 95% confidence interval (CI): 1.016 to 1.382] and HCY (OR=1.685, 95% CI: 1.009 to 2.798) levels were risk factors for left ventricular remodeling in patients with ICM ($P<0.05$). The levels of serum DD and HCY were significantly positively correlated with LVEDd and LVPW, but were significantly negatively correlated with LVEF in patients with ICM ($r=0.502, 0.518, -0.673$; $r=0.643, 0.592, -0.687, P<0.05$). **Conclusion:** Serum DD and HCY levels were significantly increased, LVEDd and LVPW were significantly increased and LVEF was significantly decreased in patients with ICM. Besides, serum DD and HCY levels were significantly correlated with left ventricular remodeling parameters in patients with ICM. DD and HCY levels are closely related to the severity of ICM.

Keywords ischemic cardiomyopathy; D-dimer; homocysteine; left ventricular remodeling

缺血性心肌病(ischemic cardiomyopathy, ICM)被视为冠心病晚期阶段,系指冠状动脉粥样硬化导致长期心肌缺血而引发的心肌弥漫性纤维化,以心绞痛、心力衰竭、心律失常等症状较为常见^[1]。现代医学研究表明:发生ICM时,由于心肌持续缺血缺氧,部分心肌出现坏死而失去收缩功能,这导致左心室壁收缩运动不协调,左心室内血液无法有效排出、心室内压力负荷随之增加,室壁在收缩与舒张期所受到的应力增加,引起整个左心室扩张和心室结构形态的变化(即左心室重构),而左心室重构不仅会严重损伤患者左心室功能,引发一系列并发症,且会增加患者病死率。如何有效预测ICM患者左心室重构成为临床关注的焦点^[2-3]。近年来,血清学标志物在心血管疾病诊断和预后评估中发挥重要作用,血清D-二聚体(D-dimer, DD)、同型半胱氨酸(homocysteine, HCY)等因子与心血管疾病的关系成为临床研究的热点。DD的临床检测主要用于血栓性疾病诊断。研究^[4]表明:心肌梗死、肺栓塞、脑梗死患者血清DD水平明显升高。HCY被视为卒中等心脑血管疾病的危险因素^[5]。目前,ICM

患者血清DD, HCY与左心室重构的关系尚未完全明确。因此,本研究旨在探讨ICM患者血清DD, HCY与左心室重构的关系,为ICM患者左心室重构的早期诊断提供参考。

1 对象与方法

1.1 对象

选择2016年6月至2019年6月成都市龙泉驿区第一人民医院收治的130例ICM患者为研究对象。男80例,女50例;年龄61~75(69.2 ± 4.1)岁。纽约心脏病协会(New York Heart Association, NYHA)心功能分级:I级35例,II级20,III级45例,IV级30例。依据冠状动脉造影结果,将ICM患者分为重构组[左心室重构(具备典型的心肌纤维化和心脏扩大等特征), $n=95$]和无重构组(无左心室重构, $n=35$)。两组性别、年龄基线资料比较,差异无统计学意义($P>0.05$)。纳入标准:有明确冠心病史,出现 ≥ 1 次心肌梗死,影像学检查发现心脏明显扩大,冠状动脉造影检查确诊为ICM;NYHA心功能分级为I~IV级;未合并室壁瘤或心律失常;患者及

其家属在自愿签署知情同意书。排除标准: 心源性休克或低血压; 合并严重肝、肾功能障碍; 重度精神疾病; 合并严重心脏瓣膜病变; 合并其他类型心脏病或其他原因所致的心脏扩大; 室间隔穿孔或心室壁瘤等。

1.2 方法

1.2.1 一般资料收集

收集患者性别、年龄、体重指数(body mass index, BMI)、高血压史、吸烟史、酗酒史、慢性呼吸系统疾病史等资料。

1.2.2 DD 检测

采集晨起空腹肘部抗凝(采用乙二胺四乙酸盐)静脉血2 mL, 以3 000 r/min离心10 min, 相对离心力为1 000~1 200 g, 分离血浆, 立即上机(迈瑞全自动凝血分析仪ExC810, 迈瑞生物医疗电子股份有限公司)检测, 试剂盒由上海长岛生物有限公司提供。

1.2.3 HCY 检测

采集晨起空腹肘部促凝静脉血5 mL, 以3 000 r/min离心10 min分离血清, 立即上机(全自动生化分析仪贝克曼AU5800, 美国)检测, 试剂盒由四川沃文特生物有限公司提供。

1.2.4 左心室重构参数检测

采用美国GE ViVid E9彩超检查患者心功能, 探头频率设为2.25~4.00 MHz, 在二维图像下获取心脏肋骨旁左心室长轴切面, 测量得到左心室舒张末期内径(left ventricular end-diastolic diameter, LVEDd), 左心室后壁厚度(left ventricular posterior wall thickness, LVPW)和左心室射血分数(left ventricular ejection fraction, LVEF), 各项指标均在呼气状态下连续获取3个心动周期, 最终取

平均值。

1.3 统计学处理

采用SPSS 20.0软件进行数据分析, 数据拟符合正态分布。计数资料以例(%)表示, 组间比较行 χ^2 检验; 计量资料以均数 \pm 标准差($\bar{x}\pm s$)表示, 不同心功能分级ICM患者血清DD、HCY水平、左心室重构参数比较行单因素方差分析或t检验, 多组间两两比较采用LSD-t检验。采用Pearson参数对ICM患者血清DD、HCY水平与左心室重构的关系进行相关性检验, 影响ICM患者左心室重构的单因素和二元logistic回归分析。以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 不同心功能分级 ICM 患者血清 DD 和 HCY 水平比较

ICM患者心功能分级越高, 血清DD和HCY水平越高, 差异有统计学意义($P<0.05$, 表1)。

2.2 不同心功能分级 ICM 患者左心室重构参数比较

ICM患者心功能分级越高, LVEDd越大, LVPW越厚而LVEF越低, 不同心功能分级患者LVEDd, LVPW和LVEF两两比较, 差异有统计学意义($P<0.05$, 表2)。

2.3 ICM 患者左心室重构的单因素分析

重构组血清DD和HCY水平明显高于无重构组($P<0.05$), 但两组其他资料比较, 差异无统计学意义($P>0.05$, 表3)。

表1 不同心功能分级ICM患者血清DD、HCY水平比较($\bar{x}\pm s$)

Table 1 Comparison of serum DD and HCY levels in ICM patients with different grades of cardiac function ($\bar{x}\pm s$)

心功能分级	<i>n</i>	DD/(mg·L ⁻¹)	HCY/(μ mol·L ⁻¹)
IV级	30	3.42 \pm 0.43 ^{*#&}	24.16 \pm 3.35 ^{*#&}
III级	45	2.68 \pm 0.29 ^{*#}	18.34 \pm 2.06 ^{*#}
II级	20	1.65 \pm 0.21 [*]	15.63 \pm 1.96 [*]
I级	35	0.43 \pm 0.19	9.04 \pm 1.01
<i>F</i>		92.654	71.028
<i>P</i>		<0.001	<0.001

与I级比较, ^{*} $P<0.05$; 与II级比较, [#] $P<0.05$; 与III级比较, [&] $P<0.05$ 。

Compared with grade I, ^{*} $P<0.05$; compared with grade II, [#] $P<0.05$; compared with grade III, [&] $P<0.05$.

表2 不同心功能分级ICM患者左室重构参数比较($\bar{x} \pm s$)Table 2 Comparison of left ventricular remodeling parameters in ICM patients with different grades of cardiac function ($\bar{x} \pm s$)

心功能分级	n	LVEDd/mm	LVPW/mm	LVEF/%
IV级	30	49.32 ± 4.45 ^{*#&}	13.17 ± 1.20 ^{*#&}	41.65 ± 4.11 ^{*#&}
III级	45	45.68 ± 4.09 ^{*#}	10.04 ± 1.01 ^{*#}	46.72 ± 4.19 ^{*#}
II级	20	41.65 ± 3.18 [*]	8.02 ± 0.97 [*]	49.64 ± 4.79 [*]
I级	35	36.43 ± 3.02	7.04 ± 0.81	52.57 ± 5.08
F		29.641	169.245	29.587
P		<0.001	<0.001	<0.001

与I级比较, *P<0.05; 与II级比较, #P<0.05; 与III级比较, &P<0.05。

Compared with grade I, *P<0.05; compared with grade II, #P<0.05; compared with grade III, &P<0.05.

表3 ICM患者左室重构的单影响因素分析

Table 3 Single factor analysis of left ventricular remodeling in patients with ICM

组别	n	男性/ [例(%)]	年龄/岁	BMI/ (kg·m ⁻²)	高血压史/ [例(%)]	吸烟史/ [例(%)]	酗酒史/ [例(%)]	慢性呼吸系 统疾病史/ [例(%)]	DD/(mg·L ⁻¹)	HCY/ (μmol·L ⁻¹)
重构组	95	63 (66.32)	69.21 ± 4.14	24.21 ± 2.12	32 (33.68)	43 (45.26)	11 (11.58)	13 (13.68)	3.49 ± 0.51	25.26 ± 3.35
无重构组	35	24 (68.57)	68.99 ± 4.20	24.18 ± 2.08	10 (28.57)	18 (51.43)	3 (8.57)	4 (11.43)	1.14 ± 0.20	12.04 ± 1.21
χ ² /t		0.059	0.268	0.072	0.306	0.390	0.241	0.115	26.467	22.758
P		0.808	0.789	0.943	0.580	0.532	0.634	0.735	<0.001	<0.001

2.4 ICM 患者左心室重构的二元 logistic 回归分析

以ICM患者是否存在左心室重构为因变量, 以单因素分析中有统计学意义的指标为自变量进行赋值[血清DD和HCY(均以实际值为准)], 经二元logistic回归分析结果提示: 血清DD和HCY水平是ICM患者左心室重构的危险因素

(P<0.05, 表4)。

2.5 ICM 患者血清 DD 和 HCY 水平与左心室重构参数的相关性分析

ICM患者血清DD和HCY水平与LVEDd和LVPW呈明显正相关, 而与LVEF呈明显负相关(P<0.05, 表5)。

表4 ICM患者左心室重构的二元logistic回归分析

Table 4 Binary logistic regression analysis of left ventricular remodeling in patients with ICM

因素	回归系数	χ ²	P	OR	95%置信区间	
					下限	上限
DD	0.321	6.169	0.013	1.102	1.016	1.382
HCY	0.449	7.121	0.008	1.685	1.009	2.798

表5 ICM患者血清DD和HCY水平与左心室重构参数的相关性分析

Table 5 Correlation analysis between serum DD, HCY levels and left ventricular remodeling parameters in patients with ICM

因素	LVEDd		LVPW		LVEF	
	r	P	r	P	r	P
DD	0.502	<0.001	0.518	<0.001	-0.673	<0.001
HCY	0.643	<0.001	0.592	<0.001	-0.687	<0.001

3 讨论

ICM发生与冠状动脉粥样硬化、心肌缺血缺氧、心肌纤维化等密切相关,以心肌细胞局部坏死、心肌肥大为主要病理特征^[5]。研究^[6]表明:左心室重构可有效反映ICM患者心脏结构以及功能改变。此外,左心室重构是ICM患者病情加重和病死率增高的主要原因,尽早有效预测ICM左心室重构对合理治疗方案的制订有重要意义。目前,临床对ICM左心室重构的诊断尚缺乏行之有效的方案。近年来,血清学标志物在心血管疾病中预测价值的研究逐渐增多。相关研究^[7-9]表明:高HCY是心血管疾病风险增加的高危因素。高瑞敏^[7]的研究表明:血清HCY水平与慢性心力衰竭患者左心室重构发生密切相关,同时在患者预后评估中有一定价值。近期,李丽琪等^[8]指出:HCY水平与原发高血压患者左心室几何构型密切相关。此外,方堃等^[9]研究发现:联合检测HCY和DD等血清因子可有效评估冠心病患者病情程度,在冠心病早期诊断和病情评估中有重要的临床价值。纵观以往文献研究,进一步探究ICM患者血清DD和HCY水平与左心室重构的关系或可为ICM患者早期诊治提供参考。

本次研究结果显示:研究组一般资料与对照组比较差异无统计学意义。校正年龄、性别、高血压史、吸烟史、酗酒史等因素的影响后,进一步研究发现:ICM患者心功能分级级别越高,血清DD和HCY水平越高,LVEDd越大,LVPW越厚,LVEF越低;不同心功能级别患者血清DD和HCY水平,LVEDd,LVPW,LVEF两两比较差异有统计学意义;初步证实了ICM患者血清DD和HCY水平明显升高,LVEDd明显增大、LVPW明显增厚,而LVEF明显降低。另外,本结果显示:血清DD(OR=1.102,95%CI:1.016~1.382)和HCY(OR=1.685,95%CI:1.009~2.798)水平是ICM患者左心室重构的危险因素,且进一步相关性分析发现:ICM患者血清DD,HCY水平与LVEDd,LVPW呈明显正相关,而与LVEF呈明显负相关,证实了ICM患者血清DD和HCY水平与左心室重构密切相关,临床中或可通过严密监测患者血清DD,HCY水平有效预测左心室重构情况。

HCY是一种含硫氨基酸,自国外学者首次提出HCY水平与动脉粥样硬化性疾病密切相关以来,一直被视为心血管疾病的高危因素^[10]。研究^[11]表明:HCY血清水平过高可抑制体内NO的合成、释放,从而严重损伤血管内皮细胞,且HCY水平过高可

致体内脂质代谢紊乱,促使血管平滑肌细胞增殖引发血小板聚集,导致机体凝血、纤溶的生理平衡被打破,引发心血管血栓的形成,从而参与冠状动脉粥样硬化斑块的形成^[12]。据文献^[13]报道:左心室重构参数LVEDd越大,LVPW越厚预示患者心肌扩大越明显,LVEF越小预示心肌功能越低。因此,ICM患者心功能分级越高,血清HCY水平越高,且血清HCY与左心室重构参数有显著相关性。DD是反映机体凝血和纤溶状态的有效指标^[14],可通过凝血以及纤溶系统等途径参与动脉粥样硬化的进展,其水平越高预示机体栓塞风险越高^[15]。DD与ICM的发生密切相关,其水平越高预示ICM患者病情越严重。因此,ICM患者血清DD水平随着心功能分级增加而明显升高,且与左心室重构参数存在明显的相关性。

综上所述,ICM患者血清DD和HCY水平与左心室重构密切相关,临床中严密监测ICM患者血清DD和HCY水平可为预测病情严重程度以及左心室重构提供有用的参考信息。但本研究同时存在研究对象来源较为集中,随访时间较短,未分析血清DD和HCY水平与ICM患者预后的关系等不足,未来还需进一步完善。

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