

冠心病患者血液 hs-CRP, ET-1, NO, NT-Pro BNP 及 D-D 水平联合检测在评估左心衰竭并发肺动脉高压的临床价值

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摘要:目的 研究冠心病(coronary heart disease, CHD)患者血清指标联合检测在评估左心衰竭并发肺动脉高压中的临床价值。方法 收集西安市第三医院心血管内科2018年10月~2020年10月84例CHD并发左心室患者临床资料,根据是否伴有肺动脉高压(pulmonary hypertension, PH)将84例患者分为观察组和对照组。比较两组患者血清相关指标[超敏C反应蛋白(high sensitive C-reactive protein, hs-CRP),内皮素-1(endothelin-1, ET-1),一氧化氮(nitric oxide, NO),氨基末端脑钠肽前体(amino-terminal pro-brain natriuretic peptide, NT-Pro BNP)和D-二聚体(D-dimer, D-D)]。采用Logistic分析CHD左心衰竭并发PH的高危因素,分析血清相关指标判断患者并发PH的价值。结果 84例患者中26例发生PH,为观察组,另58例为对照组。观察组与对照组患者血清hs-CRP, ET-1, NO, NT-Pro BNP及D-D水平比较,差异有统计学意义($t=4.98, 4.27, 5.67, 9.78$ 和 7.23 ,均 $P<0.05$)。Logistic多因素分析显示hs-CRP($\beta=0.91, 95\%CI=1.17-5.30, P=0.02$), ET-1($\beta=1.21, 95\%CI=1.56-7.15, P<0.01$), NT-Pro BNP($\beta=1.01, 95\%CI=1.32-5.73, P<0.01$)及D-D($\beta=0.62, 95\%CI=1.34-2.58, P<0.01$)是CHD左心衰竭并发PH的独立影响因素。基于多因素分析结果建立预测模型 $Y=0.91X_1+1.21X_2+1.01X_3+0.62X_4$ ($X_1=hs-CRP, X_2=ET-1, X_3=NT-Pro BNP, X_4=D-D$),受试者工作曲线(receiver operating characteristic, ROC)分析结果显示预测模型判断CHD左心衰竭并发PH的曲线下面积(area under curve, AUC)为0.80($SE=0.07, 95\%CI=0.66-0.94, P<0.01$),敏感度和特异度分别为0.85和0.73。结论 血清hs-CRP, ET-1, NT-Pro BNP及D-D联合检测用于CHD左心衰竭患者对判断其并发PH风险具有较高准确性。

关键词:冠心病;左心衰竭;肺动脉高压;联合检测

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Clinical Value of Combined Detection of Serum hs-CRP, ET-1, NO, NT-pro BNP and D-D Levels in Patients with Coronary Heart Disease in Evaluating Left Heart Failure Complicated with Pulmonary Hypertension

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Abstract: Objective To study the application value of combined detection of serum indexes in the patients of coronary heart disease (CHD) to evaluate the left heart failure complicated with pulmonary hypertension. **Methods** Clinical data of 84 patients with CHD combined with left ventricle in the Cardiovascular Medicine Department of the Third Hospital of Xi'an from October 2018 to October 2020 were collected, 84 patients were divided into observation group and control group, which accorded to the presence or absence of pulmonary hypertension (PH). The serum related indicators high sensitive C-reactive protein (hs-CRP), Endothelin-1 (ET-1), nitric oxide (NO), amino-terminal pro-brain natriuretic peptide (NT-Pro BNP), D-dimer (D-D) were compared between the two groups. The Logistic analysis was used to analyze the high risk factors of PH in patients with CHD and left heart failure, the value of RT-3DRVQ related parameters in judging PH was analyzed. **Results** There were 26 cases had PH, which was the observation group and 58 cases was the control group among the 84 patients. There were statistically significant differences in the levels of hs-CRP, ET-1, NO, NT-Pro BNP and D-D between the observation group and the control group ($t=4.98, 4.27, 5.67, 9.78$ and 7.23 , all $P<0.05$). The Logistic multivariate analysis showed that hs-CRP ($\beta=0.91, 95\%CI=1.17-5.30, P=0.02$), ET-1 ($\beta=1.21, 95\%CI=1.56-7.15, P<0.01$), NT-ProBNP ($\beta=1.01, 95\%CI=1.32-5.73, P<0.01$) and D-D ($\beta=0.62, 95\%CI=1.34-2.58, P<0.01$) were independent risk factors of PH in CHD with left heart failure. The prediction

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model $Y=0.91X_1+1.21X_2+1.01X_3+0.62X_4$ (X_1 =hs-CRP, X_2 =ET-1, X_3 =NT-Pro BNP, X_4 =D-D) was established, which based on the results of multi factor analysis. The results of receiver operating characteristic (ROC) analysis showed that the AUC of predicting model for PH in CHD with left heart failure was 0.80 (SE=0.07, 95%CI=0.66~0.94, $P<0.01$), the sensitivity and specificity were 0.85 and 0.73 respectively. **Conclusion** The combined detection of hs CRP, ET-1, NT-pro, BNP and D-D in serum has high accuracy in judging the risk of PH in CHD patients with left heart failure.

Keywords: coronary heart disease; left heart failure; pulmonary hypertension; joint detection

冠心病 (coronary heart disease, CHD) 左心衰竭是 CHD 进展的必然结果, 此类患者随着病情进展, 在缺氧和长期炎症反应条件下可累及肺血管, 使肺血管内皮受损, 进而使肺动脉发生反应性重塑^[1-2], 最终并发肺动脉高压 (pulmonary hypertension, PH)。PH 的发生将显著增加右心衰竭风险, 增加致残率和致死率^[3]。因而, PH 的预防治疗一直是 CHD 左心衰竭诊治重点。血清学指标检测具有廉价便捷优势, 可连续动态监测患者病情变化, 为临床诊疗提供依据^[4]。本研究联合检测超敏 C 反应蛋白 (high sensitive C-reactive protein, hs-CRP), 内皮素-1 (Endothelin-1, ET-1) 等常见血清指标水平, 为 PH 早期防治提供依据。报道如下。

1 材料与方法

1.1 研究对象 西安市第三医院心血管内科 2018 年 10 月~2020 年 10 月 84 例 CHD 左心衰竭患者作为研究对象。参照欧洲心脏病学会肺动脉高压指南标准^[5], 记录 84 例患者 PH 发生率。将并发 PH 的 26 例患者作为观察组, 未发生 PH 的 58 例患者作为对照组。其中观察组男性 16 例, 女性 10 例; 年龄 48.22 ± 11.30 岁; 体重指数 $20.43 \pm 1.76 \text{ kg/cm}^2$ 。对照组男性 34 例, 女性 24 例; 年龄 50.13 ± 12.84 岁; 体重指数 $20.09 \pm 1.81 \text{ kg/cm}^2$ 。两组患者性别、年龄及体重指数比较, 差异均无统计学意义 (均 $P>0.05$)。观察组患者心率 93.32 ± 10.07 次/min, 左心射血分数 (left ventricular ejection fraction, LVEF) 为 $28.42\% \pm 8.05\%$ 。对照组心率为 85.36 ± 9.64 次/min, LVEF 为 $33.32\% \pm 7.54\%$ 。两组间心率和 LVEF 水平比较, 差异均有统计学意义 ($t=3.45, 2.70$, 均 $P<0.01$)。

纳入标准: ① CHD 诊断参照美国心脏病协会推荐标准^[6]; ②左心衰竭诊断参照中华医学会心血管病学分会推荐指南标准执行^[7]; ③患者均接受实

时三维右室定量分析技术 RT-3DRVQ 检查, 且病例资料完整。

排除标准: ①不能有效配合检查或对检查不能耐受者; ②因慢性阻塞性肺疾病、肺动脉衰竭、间质性肺疾病引起的 PH; ③特发性 PH 者; ④并发有严重心律失常、肺源性心脏病及肥厚型心肌病者。

1.2 仪器和试剂 ABX pentraXL80 型全自动高效血液分析仪 (国食药监械进字 2013 第 2400387 号), 离心机采用日本 KURABO KA-2200 型血液离心机, 试剂盒均由上海信帆生物科技有限公司提供。

1.3 方法 在患者入院后 3 天内检测血清指标, 血清指标包括 hs-CRP, ET-1, 一氧化氮 (nitric oxide, NO), 氨基末端脑钠肽前体 (amino-terminal pro-brain natriuretic peptide, NT-Pro BNP) 和 D-二聚体 (D-dimer, D-D)。取患者空腹静脉血, 3 000r/min 离心 10min 后取上清液作为实验标本送检。血清 hs-CRP, D-D 采用免疫比浊法检测, ET-1 采用酶联免疫吸附法检测, NO 采用酶比色法检测, NT-Pro BNP 采用荧光免疫法检测。操作均按试剂盒说明进行。

1.4 统计学析 采用 SPSS 20.0 软件包处理数据, 计量资料以均数 \pm 标准差 ($\bar{x} \pm s$) 表示, 组间比较采用 t 检验, 计数资料以频数 (频率) 表示, 组间比较采用卡方检验, 多因素采用 Logistic 模型分析, 预测价值采用受试者工作曲线 (receiver operating characteristic, ROC) 分析, 以曲线下面积 (area under curve, AUC) >0.75 为预测价值高, $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组血清相关指标结果比较 见表 1。观察组与对照组患者 hs-CRP, ET-1, NO, NT-Pro BNP 及 D-D 水平比较, 差异均有统计学意义 (均 $P<0.05$)。

表 1 两组血清相关指标结果比较

指标	观察组 ($n=26$)	对照组 ($n=58$)	t 值	P 值
hs-CRP (mg/L)	8.14 ± 2.28	5.79 ± 1.86	4.98	<0.01
ET-1 (ng/L)	54.26 ± 8.31	45.38 ± 9.01	4.27	<0.01
NO ($\mu\text{mol/L}$)	50.78 ± 7.32	62.16 ± 8.97	5.67	<0.01
NT-Pro BNP (ng/L)	860.44 ± 167.54	562.43 ± 108.11	9.78	<0.01
D-D ($\mu\text{g/L}$)	1.52 ± 0.46	0.86 ± 0.35	7.23	<0.01

2.2 CHD左心衰竭患者并发PH风险因素分析 见表2。将可能影响CHD左心衰竭患者并发PH的相关因素纳入Logistic模型,分析结果显示hs-CRP,

ET-1, NT-Pro BNP及D-D是并发PH的独立因素($P<0.05$)。

表2 CHD左心衰竭患者并发PH风险因素分析

指标	β	SE	OR	Wald χ^2	95%CI	P
心率	1.08	0.63	2.94	2.90	0.85~10.17	0.09
LVEF	-0.67	0.41	0.51	2.75	0.23~1.13	0.10
hs-CRP	0.91	0.39	2.49	5.60	1.17~5.30	0.02
ET-1	1.21	0.39	3.34	9.64	1.56~7.15	<0.01
NO	1.04	0.66	2.84	2.51	0.78~10.34	0.11
NT-Pro BNP	1.01	0.37	2.75	7.30	1.32~5.73	<0.01
D-D	0.62	0.17	1.86	13.76	1.34~2.58	<0.01

2.3 预测模型判断PH的ROC分析 见图1。基于Logistic分析结果建立预测模型 $Y=0.91X_1+1.21X_2+1.01X_3+0.62X_4$ (X_1 =hs-CRP, X_2 =ET-1, X_3 =NT-Pro BNP, X_4 =D-D),采用ROC分析该模型判断CHD左心衰竭并发PH的价值,结果显示其AUC为0.80 (SE=0.07, 95%CI=0.66~0.94, $P<0.01$), 敏感度为0.85, 特异度为0.73。

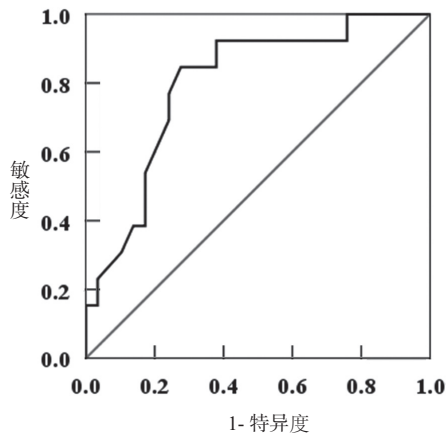


图1 预测模型判断CHD左心衰竭患者并发PH的ROC分析

3 讨论

CHD左心衰竭患者因左心房充盈压力增加,使肺静脉血流回流受阻,导致肺静脉压力相应升高,引发PH的发生^[8]。既往报道显示PH的发生使CHD患者病死风险增加2.0~5.0倍^[9]。长期以来,超声心动图作为PH的常规无创检查方法,已在临床广泛应用,超声心动图根据三尖瓣反流速度确定PH^[10]。但近年来研究显示部分CHD患者不能探测到三尖瓣反流信号^[11],这对早期诊断PH带来困难。血清指标检测能动态监测冠心病左心衰竭患者病情变化,已在临床广泛应用^[12],为CHD并发PH的早期诊断提供依据。

PH的发生使CHD左心衰竭患者右心室压力负

荷增加,并逐渐发生右室扩大和功能不全改变^[13-14],戴学庆等^[15]还证实肺动脉压力升高水平与右室扩大程度具有显著相关性。本研究显示两组hs-CRP, ET-1, NT-Pro BNP及D-D等血清指标水平差异显著,提示血清学检测有助于鉴别CHD心力衰竭是否并发PH,炎症反应在PH发生过程中扮演重要角色,是促进内皮细胞损伤和PH形成的关键环节。hs-CRP不仅能反映血管炎性程度,其水平升高多提示血管重塑的发生。另外,ET-1是内皮素的主要存在形式,其表达水平与全身炎症具有良好的相关性^[16-17]。而NT-Pro BNP作为无活性肽类残片,与右心功能不全和PH程度相关。D-D是高凝和纤溶亢进的敏感标记物,PH早期血管出现高凝状态^[18-19],因而监测D-D有助于冠心病左心衰竭并发PH的早期筛查。

本研究采用多因素分析法分析血清相关指标判断PH风险的价值,并构建模型,结果显示预测模型判断PH风险的AUC为0.80,敏感度达0.85,这对于早期筛查CHD左心衰竭并发PH的潜在因素,指导临床早期干预具有重要意义。这也提示,对于CHD左心衰竭患者,定期行血清学指标检测有助于筛查PH风险,为指导临床提供参考。

综上,联合监测血清hs-CRP, ET-1, NT-Pro BNP及D-D水平有助于评估CHD左心衰竭患者病情,为早期防治PH提供依据。

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(上接第 141 页)

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