

慢性心力衰竭患者血清 Mb, cTnI, IL-8 和 hs-CRP 水平表达与心功能分级的相关性研究

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摘要:目的 探讨慢性心力衰竭 (CHF) 患者血清肌红蛋白 (Mb)、心肌肌钙蛋白 I (cTnI)、白细胞介素-8 (IL-8) 及超敏 C 反应蛋白 (hs-CRP) 水平与心功能分级的相关性。方法 选择 2019 年 1~12 月期间于西安交通大学附属红会医院和西安市第一医院就诊的 150 例 CHF 患者作为观察组, 另选择同期健康体检的 50 例正常人群作为对照组。采用荧光酶免法检测各组研究对象的 Mb 和 cTnI 水平。采用酶联免疫吸附法和散射免疫比浊法测定 IL-8 和 hs-CRP 水平。建立受试者工作特征 (ROC) 曲线评价 Mb, cTnI, IL-8 及 hs-CRP 在诊断 CHF 中的临床意义。比较分析血清 Mb, cTnI, IL-8 及 hs-CRP 水平与心功能分级的相关性。结果 观察组和对照组的血清水平分别为 Mb($102.16 \pm 31.55 \mu\text{g/L}$ vs $31.35 \pm 12.28 \mu\text{g/L}$), cTnI($3.88 \pm 1.13 \text{ng/ml}$ vs $0.76 \pm 0.21 \text{ng/ml}$), IL-8($34.71 \pm 8.46 \text{ng/ml}$ vs $8.32 \pm 2.25 \text{ng/ml}$), hs-CRP($5.62 \pm 1.73 \text{mg/L}$ vs $0.86 \pm 0.31 \text{mg/L}$)。观察组的血清 Mb, cTnI, IL-8 及 hs-CRP 水平均显著高于对照组 ($t=15.160 \sim 21.770$, 均 $P < 0.01$)。I 级~IV 级心功能分级患者的血清水平分别为 Mb(49.17 ± 11.35 , 57.45 ± 13.74 , 96.22 ± 26.16 和 $155.74 \pm 39.37 \mu\text{g/L}$), cTnI(1.39 ± 0.47 , 2.73 ± 0.68 , 4.01 ± 1.32 和 $5.15 \pm 1.67 \text{ng/ml}$), IL-8(13.26 ± 3.77 , 19.38 ± 5.23 , 35.25 ± 9.11 和 $54.33 \pm 11.36 \text{ng/ml}$), hs-CRP(1.81 ± 0.45 , 2.21 ± 0.57 , 5.72 ± 1.64 和 $6.81 \pm 1.89 \text{mg/L}$)。不同心功能分级患者血清 Mb, cTnI, IL-8 及 hs-CRP 水平由高到低依次为: IV 级 > III 级 > II 级 > I 级, 差异均有统计学意义 ($F=66.350 \sim 134.600$, 均 $P < 0.01$)。ROC 曲线分析显示血清 Mb, cTnI, IL-8 及 hs-CRP 检测 CHF 的曲线下面积 (AUC) 分别为 Mb[0.78(95% CI 0.623~0.851)], cTnI[0.80(95% CI 0.657~0.876)], IL-8[0.69(95% CI 0.603~0.816)], hs-CRP[0.74(95% CI 0.609~0.810)], 均 $P < 0.01$ 。Mb, cTnI, IL-8 及 hs-CRP 诊断 CHF 的阳性预测值、阴性预测值、敏感度及特异度分别为 Mb(75.34, 63.34, 80.14 和 77.39), cTnI(74.15, 61.27, 75.64 和 74.88), IL-8(68.74, 59.78, 72.01 和 70.47), hs-CRP(69.46, 60.45, 70.58 和 67.46)。结论 CHF 患者血清 Mb, cTnI, IL-8 及 hs-CRP 水平均显著高于正常人群, Mb, cTnI, IL-8 及 hs-CRP 水平与患者心功能分级有正相关性。检测 Mb, cTnI, IL-8 及 hs-CRP 水平可为 CHF 的早期评估提供临床依据。

关键词: 慢性心力衰竭; 心功能分级; 肌钙蛋白 I; 肌红蛋白; 白细胞介素-8; 超敏 C 反应蛋白

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Correlation between the Expression of Serum MB, cTnI, IL-8, hs-CRP and Cardiac Function in Patients with Chronic Heart Failure

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Abstract: Objective To investigate the correlation between the levels of serum myoglobin (Mb), cardiac troponin I (cTnI), interleukin-8 (IL-8) and high sensitivity protein C (hs-CRP) in patients with chronic heart failure (CHF). **Methods** 150 patients with CHF from January 2019 to December 2019 in the Red Cross Society Hospital Affiliated to Xi'an Jiaotong University and the First Hospital of Xi'an City were selected as the observation group, and 50 healthy people in the same period were selected as the control group. The levels of Mb and cTnI were detected by enzyme immunoassay. The levels of IL-8 and hs-CRP were measured by enzyme linked immunosorbent assay and nephelometry. Receiver operating characteristic (ROC) curve was established to evaluate the clinical significance of Mb, cTnI, IL-8 and hs-CRP in the diagnosis of CHF. The correlation between serum Mb, cTnI, IL-8, hs-CRP and cardiac function was analyzed. **Results** The levels of serum in observation group and control group were Mb($102.16 \pm 31.55 \mu\text{g/L}$ vs $31.35 \pm 12.28 \mu\text{g/L}$), cTnI($3.88 \pm 1.13 \text{ng/ml}$ vs $0.76 \pm 0.21 \text{ng/ml}$), IL-8($34.71 \pm 8.46 \text{ng/ml}$ vs $8.32 \pm 2.25 \text{ng/ml}$), hs-CRP($5.62 \pm 1.73 \text{mg/L}$ vs $0.86 \pm 0.31 \text{mg/L}$). The levels of Mb, cTnI, IL-8 and hs-CRP in observation group were significantly higher than those in control group ($t=15.160 \sim 21.770$, all $P < 0.01$). The levels of Mb, cTnI, IL-8 and hs-CRP in patients with different grades of cardiac function were Mb(49.17 ± 11.35 , 57.45 ± 13.74 , 96.22 ± 26.16 and $155.74 \pm 39.37 \mu\text{g/L}$), cTnI(1.39 ± 0.47 , 2.73 ± 0.68 , 4.01 ± 1.32 and $5.15 \pm 1.67 \text{ng/ml}$), IL-8(13.26 ± 3.77 , 19.38 ± 5.23 , 35.25 ± 9.11 and $54.33 \pm 11.36 \text{ng/ml}$), hs-CRP(1.81 ± 0.45 , 2.21 ± 0.57 , 5.72 ± 1.64 and $6.81 \pm 1.89 \text{mg/L}$). The levels of Mb, cTnI, IL-8 and hs-CRP in patients with different grades of cardiac function were significantly higher than those in normal population ($F=66.350 \sim 134.600$, all $P < 0.01$). ROC curve analysis showed that the area under the curve (AUC) of Mb, cTnI, IL-8 and hs-CRP in diagnosing CHF were Mb[0.78(95% CI 0.623~0.851)], cTnI[0.80(95% CI 0.657~0.876)], IL-8[0.69(95% CI 0.603~0.816)], hs-CRP[0.74(95% CI 0.609~0.810)], all $P < 0.01$. Mb, cTnI, IL-8 and hs-CRP diagnosis CHF positive predictive value, negative predictive value, sensitivity and specificity were Mb(75.34, 63.34, 80.14 and 77.39), cTnI(74.15, 61.27, 75.64 and 74.88), IL-8(68.74, 59.78, 72.01 and 70.47), hs-CRP(69.46, 60.45, 70.58 and 67.46). **Conclusion** The levels of serum Mb, cTnI, IL-8 and hs-CRP in CHF patients were significantly higher than those in normal population, Mb, cTnI, IL-8 and hs-CRP levels were positively correlated with cardiac function grade. Detection of Mb, cTnI, IL-8 and hs-CRP levels can provide clinical basis for early evaluation of CHF.

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8.32 ± 2.25 ng/ml), hs-CRP(5.62 ± 1.73 mg/L vs 0.86 ± 0.31 mg/L), respectively. The serum levels of Mb, cTnI, IL-8 and hs-CRP in the observation group were significantly higher than those in the control group ($t = 15.160 \sim 21.770$, all $P < 0.01$). The serum levels in patients with cardiac function classification of grade I and grade IV were Mb(49.17 ± 11.35, 57.45 ± 13.74, 96.22 ± 26.16 and 155.74 ± 39.37) μg/L, cTnI(1.39 ± 0.47, 2.73 ± 0.68, 4.01 ± 1.32 and 5.15 ± 1.67) ng/ml, IL-8(13.26 ± 3.77, 19.38 ± 5.23, 35.25 ± 9.11 and 54.33 ± 11.36) ng/ml, hs-CRP(1.81 ± 0.45, 2.21 ± 0.57, 5.72 ± 1.64 and 6.81 ± 1.89 mg/l). The levels of serum Mb, cTnI, IL-8 and hs-CRP in patients with different cardiac function grades were in the order of grade IV > grade III > grade II > grade I ($F = 66.350 \sim 134.600$, all $P < 0.01$). ROC curve analysis showed that the area under curve (AUC) of serum Mb, cTnI, IL-8 and hs-CRP in detecting CHF was Mb[0.78(95% CI:0.623~0.851)], cTnI[0.80(95% CI:0.657~0.876)], IL-8[0.69(95% CI:0.603~0.816)], hs-CRP[0.74(95% CI:0.609~0.810)], all $P < 0.01$. The positive predictive value, negative predictive value, sensitivity and specificity of Mb, cTnI, IL-8 and hs-CRP in the diagnosis of CHF were Mb(75.34, 63.34, 80.14 and 77.39), cTnI(74.15, 61.27, 75.64 and 74.88), IL-8(68.74, 59.78, 72.01 and 70.47), hs-CRP(69.46, 60.45, 70.58 and 67.46), respectively.

Conclusion The levels of Mb, cTnI, IL-8 and hs-CRP were positively correlated with cardiac function. The detection of Mb, cTnI, IL-8 and hsCRP levels can provide clinical basis for early evaluation of CHF.

Keywords: chronic heart failure; cardiac function classification; troponin I; myoglobin; interleukin-8; high sensitivity C-reactive protein

慢性心力衰竭(chronic heart failure, CHF)是大部分心血管疾病的终末阶段。因此,对于CHF的早发现 and 早治疗是临床上一直最为关注的问题^[1]。临床研究表明,肌红蛋白(Mb)和心肌肌钙蛋白I(cTnI)作为重要的心肌损伤标志物可用于心力衰竭的病情评估及预后判断^[2-3]。另外的研究显示,白细胞介素-8(IL-8)和超敏C反应蛋白(hs-CRP)介导的炎症反应可能参与心肌损伤诱导心功能不全的病理过程^[4-5]。本研究通过分析150例CHF患者血液Mb, cTnI, IL-8及hs-CRP水平的变化,旨在探讨其与CHF患者心功能分级的关系,并为CHF的早期评估提供临床依据。现报道如下。

1 材料与方法

1.1 研究对象 选择2019年1月~12月期间于西安交通大学附属红会医院和西安市第一医院就诊的150例CHF患者作为观察组。其中男性82例,女性68例;年龄50~77岁,平均年龄63.78 ± 5.47岁;NYHA分级:I级32例,II级59例,III级36例,IV级23例。并发基础心脏病:冠心病66例,高血压性心脏病42例,缺血性心肌病33例,扩张型心肌病21例,风湿性心脏病14例。另选择同期健康体检的50例正常人群作为对照组,其中男性30例,女性20例;年龄50~76岁,平均年龄62.72 ± 6.23岁。两组研究对象的性别和年龄比较差异无统计学意义($P > 0.05$),具可比性。纳入标准:所有患者均符合《中国心力衰竭诊断和治疗指南2018》^[6]中CHF相关诊断标准,并按照美国纽约心脏病协会(NYHA)进行心功能分级,病程6个月以上。本研究已经获得西安交通大学附属红会医院和西安市第一医院医学伦理委员会批准,患者及家属均知情并签署同意书。排除标准:急性心力衰竭,肥厚型心肌病,急性胰腺炎、胆囊炎及慢性胆结石症,

骨骼肌损伤、急性心肌梗死、血液系统疾病、严重肝功能不全及甲状腺功能疾病,近期有卒中史及病历资料不全者。

1.2 仪器与试剂 采用雅培Ci8200生化免疫分析仪及其相应配套试剂(批号:25026hwoo, 32047hwoo)检测Mb和cTnI水平;采用贝克曼AU-680全自动生化分析仪检测IL-8和hs-CRP水平,试剂盒均购自北京九强生物科技有限公司(批号:JPC20198874, JPC20193648)。

1.3 方法

1.3.1 观察指标: ①比较两组及不同心功能分级患者入院时血液Mb, cTnI, IL-8及hs-CRP水平;②分析Mb, cTnI, IL-8及hs-CRP与心功能分级的相关性。

1.3.2 样本采集: 所有患者入院次日采集空腹静脉血5ml,取3ml血液以2 500 r/min离心15 min,分离血清后进行Mb, cTnI, IL-8及hs-CRP水平检测。Mb和cTnI采用化学发光法测定,IL-8和hs-CRP分别采用酶联免疫吸附法和散射免疫比浊法测定,检测过程均严格按照使用说明书进行。

1.4 统计学分析 采用SPSS22.0统计学软件进行数据处理,其中计量资料以均数 ± 标准差($\bar{x} \pm s$)表示, Mb, cTnI, IL-8及hs-CRP水平的两组间比较采用 t 检验,多组间比较采用单因素方差分析及 q 检验分析,绘制受试者工作特征(ROC)曲线评价Mb, cTnI, IL-8及hs-CRP在诊断CHF中的临床意义。以 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 CHF患者血清Mb, cTnI, IL-8及hs-CRP水平分析 见表1。与对照组比较,观察组血清Mb, cTnI, IL-8及hs-CRP水平均显著增高,差异有统计学意义(均 $P < 0.01$)。

表1 CHF患者血清 Mb, cTnI, IL-8 及 hs-CRP 水平分析 ($\bar{x} \pm s$)

项目	对照组 (n=50)	观察组 (n=150)	t 值	P 值
Mb ($\mu\text{g/L}$)	31.35 \pm 12.28	102.16 \pm 31.55	15.460	0.000
cTnI (ng/ml)	0.76 \pm 0.21	3.88 \pm 1.13	19.380	0.000
IL-8 (ng/ml)	8.32 \pm 2.25	34.71 \pm 8.46	21.770	0.000
hs-CRP (mg/L)	0.86 \pm 0.31	5.62 \pm 1.73	19.320	0.000

2.2 不同心功能分级 CHF 患者血清 Mb, cTnI,

表2 CHF患者不同心功能分级血清 Mb, cTnI, IL-8 及 hs-CRP 水平分析 ($\bar{x} \pm s$)

项目	I 级 (n=32)	II 级 (n=59)	III 级 (n=36)	IV 级 (n=23)	F 值	P 值
Mb ($\mu\text{g/L}$)	49.17 \pm 11.35	57.45 \pm 13.74 ^a	96.22 \pm 26.16 ^b	155.74 \pm 39.37 ^c	134.600	0.000
cTnI (ng/ml)	1.39 \pm 0.47	2.73 \pm 0.68 ^a	4.01 \pm 1.32 ^b	5.15 \pm 1.67 ^c	71.140	0.000
IL-8 (ng/ml)	13.26 \pm 3.77	19.38 \pm 5.23 ^a	35.25 \pm 9.11 ^b	54.33 \pm 11.36 ^c	103.150	0.000
hs-CRP (mg/L)	1.81 \pm 0.45	2.21 \pm 0.57 ^a	5.72 \pm 1.64 ^b	6.81 \pm 1.89 ^c	66.350	0.000

注: 与 I 级比较, ^a $P < 0.05$; 与 II 级比较, ^b $P < 0.05$; 与 III 级比较, ^c $P < 0.05$ 。

表3 ROC 曲线分析 (%)

项目	阳性预测值	阴性预测值	敏感度	特异度
Mb	75.34	63.34	80.14	77.39
cTnI	74.15	61.27	75.64	74.88
IL-8	68.74	59.78	72.01	70.47
hs-CRP	69.46	60.45	70.58	67.46

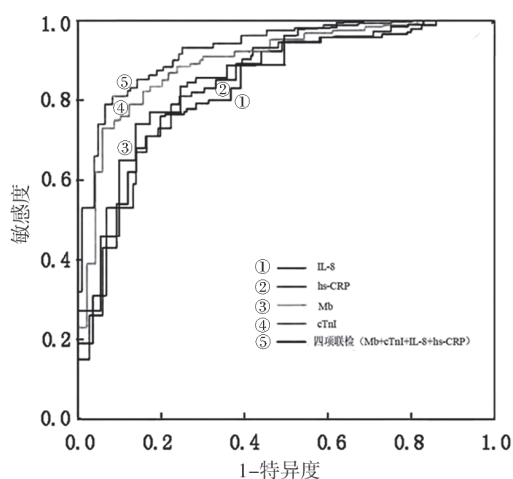


图1 Mb, cTnI, IL-8 及 hs-CRP 诊断 CHF 的 ROC 曲线

3 讨论

CHF 是一种复杂的慢性心血管疾病, 其中老年人群的发病率较高, 并且预后较差。目前的研究证实, 机体血流动力学改变导致的心室重构以及内分泌系统的一系列病理变化可能是引起 CHF 发病的主要机制^[7-9]。因此, 如何快速准确诊断 CHF, 对于提高患者的临床疗效, 改善预后具有重要意义。

研究发现心肌损伤是 CHF 的典型特征, Mb 和 cTnI 是临床上评价心肌受损程度的重要标志物。Mb 是机体内的一种储氧蛋白, cTnI 为一种肌肉

IL-8 及 hs-CRP 水平分析 见表 2。心功能 I ~ IV 级患者血清 Mb, cTnI, IL-8 及 hs-CRP 水平均依次增高, 差异有统计学意义 (均 $P < 0.01$)。

2.3 ROC 曲线分析 Mb, cTnI, IL-8 及 hs-CRP 的曲线下面积 (AUC) 分别为 0.78 (95%CI 0.623~0.851), 0.80 (95%CI 0.657~0.876), 0.69 (95%CI 0.63~0.816), 0.74 (95%CI 0.609~0.810), 均 $P < 0.01$ 。Mb, cTnI, IL-8 及 hs-CRP 的阳性预测值、阴性预测值、敏感度及特异度见表 3 和图 1。

收缩调节蛋白, 心肌细胞受损时常释放大量的 Mb 和 cTnI, 导致血液 Mb 和 cTnI 水平明显增高^[10]。研究发现, 随着心肌受损程度的加重, cTnI 水平持续增高^[11]。另有报道认为, 老年 CHF 患者入院时血浆 Mb 水平明显高于正常人群, 随着 NYHA 心功能分级的加重, Mb 水平均逐渐升高^[12]。以上临床诸多研究表明了 Mb 和 cTnI 对于 CHF 诊断及病情评估的重要性。本研究结果也印证了上述文献的观点。同时还显示随着心功能分级的增加 CHF 患者血清 Mb, cTnI 水平逐渐增高。提示 Mb 和 cTnI 水平的差异性变化与 CHF 患者的心功能损害程度有关。但值得注意的是, 外周血液 Mb 水平在细胞损伤 2~3h 出现增高, 而在疾病恢复期其水平则出现快速下降。部分学者认为针对心电图没有明显改变的急性心肌梗死患者, Mb 阴性可进行有效地排除诊断^[13]。因此, Mb 可能更适合于急性心肌损伤的早期诊断以及心功能衰竭的风险评估。

研究表明, 炎症反应及免疫应答是 CHF 的重要机制之一, 其始终伴随在心功能衰竭的发展过程中^[14]。IL-8 为趋化因子家族的重要成员, 主要由上皮细胞和巨噬细胞分泌。IL-8 通过激活中性粒细胞进而发挥促炎作用。临床研究显示 IL-8 与 CHF 患者的心肌损伤程度明显相关^[15]。hs-CRP 是一种急性时相反应蛋白, 心力衰竭患者体内的炎症反应诱导 hs-CRP 被大量释放到血液中, 造成患者血液 hs-CRP 水平迅速升高。研究显示 IL-8 和 hs-CRP 与 CHF 的发生、发展和预后存在紧密联系^[16-17]。本研究结果显示, 观察组患者血清 IL-8 和 hs-CRP 水平明显高于对照组。这与 CHAI 等^[18]的相关报道结果相符。本研究进一步分析显示随着心功能分级增

高,CHF患者外周血液IL-8及hs-CRP水平也随之增高。提示IL-8和hs-CRP与CHF患者心肌损伤程度密切相关。

ROC曲线分析结果显示Mb, cTnI, IL-8和hs-CRP对CHF诊断均具有临床意义。四项指标对CHF诊断有较高的阳性预测值、阴性预测值、敏感度及特异度。提示四项指标联合检测可用于CHF的诊断及临床疗效监测。

综上所述,血清Mb, cTnI, IL-8和hs-CRP水平与CHF患者心功能损伤的严重程度相关。通过联合检测上述四项指标可为CHF的早期诊断、病情及预后评估提供指导依据。

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