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急性心肌梗死患者血浆 BNP、NT-proBNP、MYO 及 cTnI 水平的表达及临床意义 *

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摘要 目的:探讨急性心肌梗死患者血浆 B 型利钠肽(BNP)、N-末端 B 型利钠肽原(NT-proBNP)、肌红蛋白(MYO)及心肌肌钙蛋白 I(cTnI)的表达及临床意义。**方法:**选择 2015 年 8 月至 2016 年 8 月我院收治的 162 例急性心肌梗死患者记为观察组,另选择 162 例同期于我院健康体检志愿者为对照组进行对比研究。应用免疫分离法检测两组血浆 BNP、NT-proBNP、MYO 及 cTnI 水平。对比两组血浆 BNP、NT-proBNP、MYO 及 cTnI 的表达水平,以及 BNP、NT-proBNP、MYO、cTnI 单独检测和联合检测在急性心肌梗死诊断中的灵敏度及特异性,并分析各指标之间的相关性。**结果:**观察组血浆 BNP、NT-proBNP、MYO 及 cTnI 水平均高于对照组,差异有统计学意义($P<0.05$)。四项联合检测的灵敏度分别高于血浆 BNP、NT-proBNP、MYO 及 cTnI 单独检测,特异性分别高于血浆 NT-proBNP、MYO 单独检测,差异有统计学意义($P<0.05$)。四项联合检测的特异性分别高于血浆 BNP、cTnI 单独检测,但差异无统计学意义($P>0.05$)。通过 Spearman 相关性分析显示,观察组血浆 BNP、NT-proBNP、MYO 及 cTnI 各指标水平之间呈正相关($P<0.05$)。**结论:**血浆 BNP、NT-proBNP、MYO 及 cTnI 在急性心肌梗死中具有明显高表达,且四项联合检测的灵敏度及特异性较高,各指标之间存在正相关关系,可为急性心肌梗死早期诊断提供科学的依据,值得临床推广。

关键词:急性心肌梗死;B 型利钠肽;N-末端 B 型利钠肽原;肌红蛋白;心肌肌钙蛋白 I

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The Expression Levels and Clinical Significance of Plasma BNP, NT-proBNP, MYO and cTnI in Patients with Acute Myocardial Infarction*

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ABSTRACT Objective: To investigate the expression and clinical significance of plasma B type natriuretic peptide (BNP), N-terminal B type natriuretic peptide (NT-proBNP), myoglobin (MYO) and cardiac troponin I (cTnI) in patients with acute myocardial infarction. **Methods:** 162 patients with acute myocardial infarction who were admitted in our hospital from August 2015 to August 2016 were selected as the observation group. In addition, 162 healthy volunteers in our hospital at the same time were selected as the control group for comparison study. The levels of plasma BNP, NT-proBNP, MYO and cTnI in two groups were detected by immuno isolation. The expression levels of plasma BNP, NT-proBNP, MYO and cTnI were compared in two groups, the sensitivity and specificity of BNP, NT-proBNP, MYO and cTnI separate detection and combined detection in the diagnosis of acute myocardial infarction were compared, and the correlation between the indexes was analyzed. **Results:** The levels of plasma BNP, NT-proBNP, MYO and cTnI in the observation group were higher than those in the control group, and the difference was statistically significant ($P<0.05$). The sensitivity of combined detection of four was higher than that of plasma BNP, NT-proBNP, MYO and cTnI respectively, the specificity was higher than that of plasma NT-proBNP, MYO respectively, the difference was statistically significant ($P<0.05$). The specificity of combined detection of four was higher than that of plasma BNP, cTnI respectively, but the difference was not statistically significant ($P>0.05$). The Spearman correlation analysis showed that there was a positive correlation between the levels of plasma BNP, NT-proBNP, MYO and cTnI in the observation group ($P<0.05$). **Conclusion:** The levels of plasma BNP, NT-proBNP, MYO and cTnI are highly expressed in patients with acute myocardial infarction, the sensitivity and specificity of combined detection of four are high, there is a positive correlation between the indexes, and it can provide scientific basis for early diagnosis of acute myocardial infarction, which is worthy of clinical popularization.

Key words: Acute myocardial infarction; B-type natriuretic peptide; N-terminal B-type natriuretic peptide; Myoglobin; Cardiac troponin

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前言

急性心肌梗死是在冠状动脉粥样硬化的基础上,因冠状动脉腔突然阻塞,从而引起冠状动脉急性、持续的缺氧和缺血所导致的心肌坏死^[1,2]。临床发病后多表现为不同程度的持续性胸骨后疼痛,同时有数据显示,超过 75% 的患者在起病 1-2 周内会发生心律失常,并且多数发生在 24h 内,在病初几小时内极易发生急性心力衰竭及休克,增加急性心肌梗死死亡风险^[3,4]。据急性心肌梗死病原学研究资料发现,我国急性心肌梗死发病率呈逐渐升高趋势,每年新发病例约达 50 万,严重影响患者生命安全^[5]。提高急性心肌梗死早期诊断准确性是避免疾病发展、降低死亡率的关键^[6]。血浆 B 型利钠肽(B-type natriuretic peptide,BNP)属于天然激素,由人体心肌细胞合成的,主要于心室表达,是突发心血管疾病的危险因子^[7,8]。N-末端 B 型利钠肽原(N-terminal B-type natriuretic peptide,NT-proBNP)由 BNP 转录生成,与 BNP 呈正相关性,具有半衰期长,稳定性高等特点^[9,10]。肌红蛋白(myoglobin,MYO)分子量小,扩散速度快,在心肌及骨骼肌细胞中大量存在,是心肌损伤最佳诊断标志物^[11,12]。心肌肌钙蛋白 I(cardiac troponin I,cTnI)属于心肌收缩调节蛋白,通过与肌球蛋白相互调节介导,维持人体心肌正常功能,具有较高的阳性诊断价值^[13,14]。因此,本研究在急性心肌梗死患者中进行血浆 BNP、NT-proBNP、MYO 及 cTnI 检测,并分析其表达情况及临床意义。现将结果整理如下。

1 资料与方法

1.1 一般资料

选择 2015 年 8 月至 2016 年 8 月我院收治的 162 例急性心肌梗死患者为观察组,纳入标准:(1)所有患者均经影像学、心肌标志物等联合检查确诊为急性心肌梗死^[15],诊断标准如下:起病急骤,疼痛、胸闷时间长,疼痛位于心前区或胸骨处,可向左臂、左颈放射,为压榨性疼痛,患者常常伴随濒死感;心电图演变:面向梗塞区导联 ST 段 Q 波出现异常抬高,ST 段抬高部分连接 T 波呈单向曲线,R 波降低,背向梗塞区导联 ST 段降低和 R 波升高;血清酶浓度先升高后降低,发病前 6 小时出现

血清肌酸磷酸激酶,24 小时后达到高峰,2-4d 后消失,达 92% 阳性率;(2)患者或家属均签署知情同意书。排除标准:(1)其他类型心脏疾病者;(2)合并严重肝、肾功能障碍者;(3)精神异常者;(4)免疫功能障碍者^[6];(5)不配合研究者。其中男 86 例,女 76 例;年龄 54-74 岁,平均年龄(63.43±4.51)岁。另选择 162 例于我院行健康体检志愿者为对照组,其中男 84 例,女 78 例;年龄 53-76 岁,平均年龄(62.25±4.39)岁。两组一般资料比较差异无统计学意义($P>0.05$),具有可比性。本研究经医院伦理委员会审核通过。

1.2 方法

观察组患者于入院后抽取清晨空腹静脉血,对照组于体检当日抽取,采集血量均为 3 mL,以 3000 r/min 的速度进行离心,离心半径 6 cm,时间为 10 min,提取血浆,应用免疫分离法进行血浆 BNP、NT-proBNP、MYO 及 cTnI 水平检测,试剂盒由上海森雄科技实业有限公司提供,所有操作均严格按照试剂盒说明书进行。

1.3 观察指标

对比所有研究对象血浆 BNP、NT-proBNP、MYO、cTnI 的表达水平,以及 BNP、NT-proBNP、MYO、cTnI 单独检测和联合检测在急性心肌梗死诊断中的灵敏度及特异性,并分析各指标之间的相关性。灵敏度 = 真阳 / (真阳 + 假阴) × 100%,特异性 = 真阴 / (假阳 + 真阴) × 100%。通过 Spearman 相关性分析观察组血浆 BNP、NT-proBNP、MYO 及 cTnI 的相关性。

1.4 统计学方法

采用 SPSS 22.0 软件进行统计分析,NT-proBNP 水平等计量资料以($\bar{x} \pm s$)描述,行 t 检验,计数资料用例(n)、占比(%)描述,行 χ^2 检验,采用 Spearman 相关性分析进行分析,设置检验水准 $\alpha=0.05$ 。

2 结果

2.1 两组心肌标志物检测水平比较

观察组血浆 BNP、NT-proBNP、MYO 及 cTnI 水平均高于对照组,差异有统计学意义($P<0.05$)。见表 1。

表 1 两组心肌标志物检测水平比较($\bar{x} \pm s$)

Table 1 Comparison of the levels of myocardial markers in two groups ($\bar{x} \pm s$)

Groups	n	BNP (ng/L)	NT-proBNP (ng/L)	MYO (g/L)	cTnI (g/L)
Control group	162	50.92±9.73	115.89±87.34	32.79±26.27	0.06±0.03
Observation group	162	195.33±76.89	2074.35±927.34	193.74±101.25	8.89±4.73
t		23.716	26.762	19.584	23.760
P		0.000	0.000	0.000	0.000

2.2 两组血浆 BNP、NT-proBNP、MYO 及 cTnI 单独及联合检测灵敏度及特异性比较

在急性心肌梗死诊断中,四项联合检测的灵敏度分别高于血浆 BNP、NT-proBNP、MYO 及 cTnI 单独检测,特异性分别高于血浆 NT-proBNP、MYO 单独检测,差异有统计学意义($P<0.05$),四项联合检测的特异性分别高于血浆 BNP、cTnI 单独检

测,但差异无统计学意义($P>0.05$)。见表 2。

2.3 观察组血浆 BNP、NT-proBNP、MYO 及 cTnI 相关性比较

通过 Spearman 相关性分析显示,观察组血浆 BNP、NT-proBNP、MYO 及 cTnI 各指标水平之间呈正相关($P<0.05$)。见表 3。

表 2 两组血浆 BNP、NT-proBNP、MYO 及 cTnI 单独及联合检测灵敏度及特异性比较

Table 2 Sensitivity and specificity of BNP, NT-proBNP, MYO, and cTnI separate and combined detection in two group

Indexes	True positive(n)	False negative(n)	False positive(n)	True negative(n)	Sensitivity(%)	Specificity(%)
BNP	139	23	13	149	85.80 ^a	91.98
NT-proBNP	140	22	19	143	86.42 ^a	88.27 ^a
MYO	137	25	49	113	84.57 ^a	69.75 ^a
cTnI	134	28	11	151	82.72 ^a	93.21
Combined detection	158	4	9	153	97.53	94.44

Note: compared with combined detection, ^a $P < 0.05$.

表 3 观察组血浆 BNP、NT-proBNP、MYO 及 cTnI 相关性比较

Table 3 Correlation of plasma BNP, NT-proBNP, MYO, and cTnI in the observation group

Indexes	NT-proBNP		MYO		cTnI	
	r	P	r	P	r	P
BNP	0.336	0.039	0.437	0.011	0.224	0.019
NT-proBNP	-	-	0.259	0.021	0.298	0.033
MYO	-	-	-	-	0.358	0.025

3 讨论

急性心肌梗死是临床常见的心血管疾病,具有起病急、进展快、死亡率高特点,而尽早进行诊断是避免疾病恶化、提高治愈率、改善预后的重要前提^[16,17]。因此,需寻求较为完整的、应用价值高的诊断体系,以利于急性心肌梗死的早期诊断。心肌标志物检测是心血管疾病早期诊断的常用手段,其中血浆 BNP、NT-proBNP 在急性心肌梗死中具有较高的应用价值^[18]。据研究显示^[19],MYO 在急性心肌梗死发病后开始升高,12h 内达高峰,随时间的推移而恢复正常,因此可作为观察溶栓治疗、诊断急性心肌梗死的重要指标。cTnI 半衰期长,可达 15d,利于回顾性检测^[20],并且在心肌梗死发生 1.5h 后即可在血浆中检测出,可应用于急性心肌梗死发生早期诊断。血清标志物检测标本采集简便,速度较快,可尽早根据检测结果采取合适的对症治疗干预措施,以降低急性心肌梗死猝死的风险^[21]。

本研究结果显示,观察组血浆 BNP、NT-proBNP、MYO 及 cTnI 水平均高于对照组($P < 0.05$),说明血浆 BNP、NT-proBNP、MYO 及 cTnI 在急性心肌梗死中均具有明显高表达,可应用于临床诊断中。其中当出现左心功能异常时,BNP 会在心肌内快速合成并释放,从而进入血液循环,故在健康人群血浆中 BNP 水平极低,NT-proBNP 水平随着 BNP 水平的升高而升高,并且其与心功能不全的严重程度关系密切^[22,23]。MYO 主要存在于心肌及骨骼肌细胞中,具有结合和释放氧气的功能,有助于氧在肌肉细胞中的分布,是最早进入血浆的心肌标志物,当心脏疾病发生时,MYO 也会随之升高^[24]。cTnI 是心肌损伤调控蛋白,在心肌细胞膜完整时,cTnI 不会进入血液循环,当发生心肌损伤时,cTnI 才释放入血液循环,且 cTnI 浓度与心肌受损程度呈正相关^[25,26]。同时,四项联合检测的灵敏度分别高于血浆 BNP、NT-proBNP、MYO 及 cTnI 单独检测,特异性分别高于血浆 NT-proBNP、MYO 单独检测($P < 0.05$),四项联合检测的特异性

分别高于血浆 BNP、cTnI 单独检测,但差异无统计学意义($P > 0.05$),说明联合检测在急性心肌梗死早期诊断中应用价值更高,可尽可能避免漏诊及误诊,提高早期诊断的准确性。其原因为血浆 BNP、NT-proBNP、MYO 及 cTnI 单独检测仍存在明显的不足,急性心肌梗死发病初几小时多伴有急性心力衰竭,致使 BNP 在急性心肌梗死早期诊断中具有较高的特异性低于联合检测,MYO 不仅在心肌损伤时有所表达,在骨骼肌发生损伤时表达也会明显增高,因此其心肌特异性较低,需联合其他检测进行心肌损伤诊断^[27,28],cTnI 水平仅仅维持半个月,所以对于检测急性心肌梗死也存在一定的局限性。因此,需进行心肌标志物联合检测,以互相弥补各指标之间不足,提高早期诊断的准确性及特异性^[29,30]。并且心肌标志物检测在心肌梗死临床诊断中灵敏度及特异性仍未达到百分之百,存在一定误诊或漏诊风险,因此还需与影像学检查联合进行诊断,以最大限度提高早期诊断准确性。本研究通过 Spearman 相关性分析显示,观察组血浆 BNP、NT-proBNP、MYO 及 cTnI 各指标水平之间呈正相关($P < 0.05$),说明 BNP、NT-proBNP、MYO 及 cTnI 联合检测在急性心肌梗死早期诊断中优势显著,对患者预后评估更具有优势。

综上所述,急性心肌梗死患者血浆 BNP、NT-proBNP、MYO 及 cTnI 的表达偏高,且上述指标具有相关性,四项联合检测可提高灵敏度及特异性,可作为早期诊断急性心肌梗死的标志物,以改善疾病预后,降低病死发生的风险。

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