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不同病情冠心病患者血清心型脂肪酸结合蛋白 与颈动脉内膜中层厚度的关系分析*

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摘要 目的:探讨不同病情冠心病患者血清心型脂肪酸结合蛋白(H-FABP)与颈动脉内膜中层厚度(IMT)的关系。**方法:**选择内蒙古科技大学包头医学院第一附属医院老年科收治的冠心病患者 60 例,其中稳定型心绞痛(SAP)和急性冠脉综合征(ACS)各 30 例,根据冠状动脉病变支数将患者分为单支病变组 19 例、双支病变组 19 例和多支病变组 22 例;根据患者冠状动脉血管狭窄程度分为轻度病变组 22 例、中度病变组 17 例和重度病变组 21 例,选择同期健康体检者 30 例作为对照组。比较各组颈动脉 IMT 及血清 H-FABP 水平,并分析其相关性。**结果:**ACS 组颈动脉 IMT 及血清 H-FABP 水平显著高于 SAP 组和对照组,SAP 组颈动脉 IMT 及血清 H-FABP 水平显著高于对照组($P<0.05$)。不同冠状动脉病变支数、病变程度冠心病患者颈动脉 IMT 及血清 H-FABP 水平整体比较差异有统计学意义($P<0.05$),多支病变组和双支病变组血清 H-FABP 水平比较无统计学意义($P>0.05$)。Spearman 相关分析显示,冠心病患者血清 H-FABP 水平与颈动脉 IMT 呈正相关($r=0.754, P<0.05$)。**结论:**冠心病患者血清 H-FABP 水平与颈动脉 IMT 异常升高,其水平随冠状动脉病变程度加重而升高,且两者呈正相关。

关键词:病情;冠心病;心型脂肪酸结合蛋白;颈动脉内膜中层厚度;相关性

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Analysis of the Relationship between Serum Heart Type Fatty Acid Binding Protein and Carotid Intima-media Thickness in Patients with Different Conditions of Coronary Heart Disease*

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ABSTRACT Objective: To investigate the relationship between serum heart type fatty acid binding protein (H-FABP) and carotid intima-media thickness in patients with different conditions of coronary heart disease. **Methods:** 60 patients with coronary heart disease who were treated in Geriatrics Department of The First Affiliated Hospital of Baotou Medical College of Inner Mongolia University of Science and Technology were selected, the patients included 30 patients with stable angina pectoris (SAP) and 30 patients with acute coronary syndrome (ACS), they were divided into single-vessel lesion group (19 cases), double-vessel lesion group (19 cases) and multi-vessel lesion group (22 cases) according to the number of coronary artery lesions. The patients were divided into mild lesion group (22 cases), moderate lesion group (17 cases) and severe lesion group (21 cases) according to the degree of coronary artery stenosis. 30 healthy people in the same period were selected as control group. The carotid IMT and serum level of H-FABP were compared in each group, and their correlation was analyzed. **Results:** The carotid IMT and serum level of H-FABP in the ACS group were significantly higher than those in the SAP group and the control group. The carotid IMT and serum level of H-FABP in the SAP group were significantly higher than those in the control group ($P<0.05$). The carotid IMT and serum level of H-FABP in patients with different coronary artery lesions and degree of coronary artery disease had statistical significance($P<0.05$). There was no significant difference in the level of serum H-FABP between patients with multi-vessel lesions and patients with double vessel lesions($P>0.05$). Spearman correlation analysis showed that serum level of H-FABP was positively correlated with carotid IMT in patients with coronary heart disease ($r=0.754, P<0.05$).

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Conclusion: The level of serum H-FABP and carotid IMT in patients with coronary heart disease increased abnormally, and its level is increased with the degree of coronary artery disease, and there is a positive correlation between them.

Key words: Condition; Coronary heart disease; Cardiac fatty acid binding protein; Carotid intima-media thickness; Correlation

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前言

当今社会,人们精神压力较大,加之生活方式和饮食结构的改变,冠心病已经成为我国发病率较高的疾病。有报道显示,目前我国居民冠心病患病率约为 0.77~1.24%,患病人数超过 1100 万,死亡率为 110.67/10 万^[1,2],冠心病已成为危害人类健康的“第一杀手”。冠心病的主要发病基础是冠状动脉粥样硬化。研究表明^[3],动脉粥样硬化是一种全身弥漫性病理变化,不仅发生于冠状动脉,也发生于颈动脉,且颈动脉粥样硬化发病往往早于冠状动脉粥样硬化,因此通过检测颈动脉内膜-中层厚度(Intima-media thickness, IMT)可能间接反映冠状动脉病变程度。心型脂肪酸结合蛋白(Heart type fatty acid binding Protein, H-FABP)是一种可溶性小分子蛋白,主要存在于心肌细胞浆内,是心肌细胞内脂肪酸运输和代谢的重要载体^[4,5]。有研究表明^[6],当心肌细胞受损后 H-FABP 可以从损伤的心肌细胞快速释放到血液中,是急性心肌梗死的敏感指标。本研究分析冠心病患者血清 H-FABP 与 IMT 的关系,旨在为冠心病的筛查及严重程度的评估提供依据,现作以下报道。

1 资料与方法

1.1 一般资料

选择 2017 年 5 月至 2018 年 4 月内蒙古科技大学包头医学院第一附属医院老年科收治的冠心病患者 60 例,纳入标准:(1)所有患者均符合中华医学会制定的冠心病诊断标准^[7],并经冠状动脉造影确诊;(2)患者初次就诊,病历资料齐全;(3)患者及其家属对本研究知情同意,签署知情同意书。排除标准:(1)合并先天性心脏病、持续性心房纤颤、严重心脏瓣膜病、心肌病等患者;(2)合并恶性肿瘤、感染、风湿、类风湿及免疫性疾病者;(3)低血压休克、严重电解质紊乱患者;(4)妊娠期或哺乳期妇女。其中稳定型心绞痛(Stable angina pectoris, SAP)30 例作为 SAP 组,急性冠脉综合征(Acute coronary syndrome, ACS)30 例作为 ACS 组,另选择同期健康体检者 30 例作为对照组,三组年龄、性别构成等基线资料比较差异无统计学意义($P>0.05$),

具有可比性,见表 1。本研究经我院伦理委员会同意。

1.2 方法

1.2.1 冠状动脉造影及分组 所有冠心病患者均采用 Judkins 法经股动脉或桡动脉入路穿刺,进行冠状动脉造影检查,并记录左主干、右冠状动脉、左前降支、回旋支病变情况,当血管的内径狭窄 $\geq 50\%$ 判断为血管狭窄^[8],计算每名患者冠状动脉病变支数,分为单支病变组 19 例、双支病变组 19 例和多支病变组 22 例。根据患者冠状动脉血管狭窄程度分为轻度病变组 22 例($50\% \leq$ 冠状动脉血管狭窄 $<75\%$)、中度病变组 17 例($75\% \leq$ 冠状动脉血管狭窄 $<90\%$)和重度病变组 21 例(冠状动脉血管狭窄 $\geq 90\%$)^[9]。

1.2.2 血清 H-FABP 检测 冠心病患者于入院即刻采集外周静脉血 5 mL,对照组于体检当日采集外周静脉血 5 mL,经 3000 r/min 离心 5 min,离心半径 12 cm,分离血清,置于 -20°C 低温保存集中检测,应用双抗体酶联免疫吸附法测定血清 H-FABP 水平,试剂盒购自美国 RD(安迪)公司,严格按照试剂盒说明进行操作。

1.2.3 颈动脉超声检查 应用飞利浦 iU22 彩色超声多普勒检测受试者双侧 IMT,探头频率设置为 7~12 MHz,患者取仰卧位,肩部垫高,头后仰转向对侧,将探头置于颈总动脉处检测其分叉近心端 2 cm 处 IMT,左右各测 3 个心动周期,取平均值,当颈动脉 IMT ≥ 1.0 mm 提示颈动脉粥样硬化^[10]。

1.3 统计学方法

使用 SPSS25.0 软件进行统计学分析,计量资料以($\bar{x} \pm s$)表示,多组数据比较应用单因素方差分析,两组比较实施 t 检验,计数资料以率表示,比较应用卡方检验,应用 Spearman 相关分析冠心病患者血清 H-FABP 水平与 IMT 的相关性, $P<0.05$ 记作差异有统计学意义。

2 结果

2.1 SAP 组、ACS 组和对照组基线资料比较

SAP 组、ACS 组和对照组年龄、性别构成、BMI、TC、TG、LDL-C、HDL-C 比较差异无统计学意义($P>0.05$),见表 1。

表 1 SAP 组、ACS 组和对照组基线资料比较

Table 1 Comparison of baseline data in SAP group, ACS group and control group

Projects	SAP group(n=30)	ACS group(n=30)	Control group(n=30)	F/ χ^2	P
Age (years)	66.42 $\pm$ 8.72	67.31 $\pm$ 9.32	65.73 $\pm$ 9.38	1.275	0.282
Gender (male/female)	19/11	19/11	18/12	0.095	0.954
BMI(kg/m ²)	24.35 $\pm$ 1.48	24.73 $\pm$ 1.57	23.78 $\pm$ 1.31	0.734	0.423
TG(mmol/L)	1.56 $\pm$ 0.51	1.57 $\pm$ 0.44	1.52 $\pm$ 0.42	0.062	0.975
TC(mmol/L)	4.75 $\pm$ 1.14	4.81 $\pm$ 1.18	4.70 $\pm$ 1.12	0.128	0.820
LDL-C(mmol/L)	3.35 $\pm$ 0.81	3.31 $\pm$ 0.85	3.25 $\pm$ 1.01	0.124	0.823
HDL-C(mmol/L)	1.07 $\pm$ 0.23	1.02 $\pm$ 0.25	1.10 $\pm$ 0.18	0.089	0.973

2.2 三组颈动脉 IMT 及血清 H-FAB 水平比较

三组颈动脉 IMT 及血清 H-FAB 水平比较差异有统计学意义($P<0.05$), ACS 组颈动脉 IMT 及血清 H-FAB 水平显著高

于 SAP 组和对照组, SAP 组颈动脉 IMT 及血清 H-FAB 水平显著高于对照组($P<0.05$), 见表 2。

表 2 SAP 组、ACS 组和对照组颈动脉 IMT 及血清 H-FAB 水平比较

Table 2 Comparison of carotid IMT and serum H-FAB level in SAP group, ACS group and control group

Groups	n	Carotid IMT(mm)	H-FABP(ng/mL)
SAP group	30	1.25± 0.29*	7.51± 1.13*
ACS group	30	1.47± 0.31* [#]	12.61± 2.75* [#]
Control group	30	0.71± 0.12	5.28± 1.59
F		3.643	8.751
P		0.012	0.000

Note: Compared with control group, * $P<0.05$; compared with SAP group, [#] $P<0.05$.

2.3 不同冠状动脉病变支数冠心病患者颈动脉 IMT 及血清 H-FAB 水平比较

不同冠状动脉病变支数冠心病患者颈动脉 IMT 及血清 H-FABP 水平比较差异有统计学意义($P<0.05$), 多支病变组、双

支病变组颈动脉 IMT 及血清 H-FABP 水平显著高于单支病变组, 多支病变组颈动脉 IMT 显著高于双支病变组($P<0.05$), 多支病变组和双支病变组血清 H-FABP 水平比较差异无统计学意义($P>0.05$), 见表 3。

表 3 不同冠状动脉病变支数冠心病患者颈动脉 IMT 及血清 H-FAB 水平比较

Table 3 Comparison of carotid IMT and serum H-FAB level in patients with coronary heart disease with different number of coronary artery lesions

Groups	n	Carotid IMT(mm)	H-FABP(ng/mL)
Single vessel lesion group	19	1.13± 0.15	7.74± 1.52
Double-vessel lesion group	19	1.34± 0.28*	10.51± 3.27*
Multi-vessel lesion group	22	1.58± 0.43* [#]	11.67± 3.71*
F	-	3.433	4.409
P	-	0.026	0.042

Note: Compared with single vessel lesion group, * $P<0.05$; Compared with double-vessel lesion group, [#] $P<0.05$.

2.4 不同病变程度冠心病患者颈动脉 IMT 及血清 H-FABP 水平比较

不同病变程度患者颈动脉 IMT 及血清 H-FABP 水平比较差异有统计学意义($P<0.05$), 重度病变组颈动脉 IMT 及血清

H-FABP 水平显著高于中度病变组和轻度病变组, 中度病变组患者颈动脉 IMT 及血清 H-FABP 水平显著高于轻度病变组($P<0.05$), 见表 4。

表 4 不同病变程度冠心病患者颈动脉 IMT 及血清 H-FABP 水平比较

Table 4 Comparison of carotid IMT and serum H-FAB level in patients with coronary heart disease of different pathological degrees

Groups	n	Carotid IMT(mm)	H-FABP(ng/mL)
Mild lesion group	22	1.13± 0.14	7.51± 1.15
Moderate lesion group	17	1.32± 0.28*	9.22± 2.11*
Severe lesion group	21	1.64± 0.43* [#]	13.41± 2.72* [#]
F	-	3.633	9.409
P	-	0.024	0.000

Note: Compared with moderate lesion group, * $P<0.05$; compared with mild lesion group, [#] $P<0.05$.

2.5 冠心病患者血清 H-FABP 水平与颈动脉 IMT 的相关性分析

Spearman 相关分析显示, 冠心病患者血清 H-FABP 水平与颈动脉 IMT 呈正相关($r=0.754$, $P=0.008$)。

3 讨论

研究表明, 动脉粥样硬化是一种全身弥漫性病理变化, 病变可以累及全身多处血管床和脏器^[1]。其中冠状动脉、主动脉、颈动脉、肾动脉和脑动脉是最常累及的部位^[12]。当血管发生动脉粥样硬化后可表现为内-中膜脂质、血液成分和复合糖类沉积, 血管平滑肌细胞增殖、胶原纤维增多, 可伴有坏死钙化

等^[13-15]。颈动脉粥样硬化与冠状动脉粥样硬化有着共同的病因、发病机制和病理基础,且颈动脉粥样硬化发病往往早于冠状动脉粥样硬化^[16]。但目前对颈动脉 IMT 是否具有对冠心病事件的预测价值仍存在争议。Zhao XX 等^[17]报道,颈动脉 IMT 对急性冠心病事件预测价值较低。Timóteo AT 等也报道^[18]年轻人群颈动脉 IMT 对冠心病预测价值较低。而 Franceschini N 等^[19]通过 8 个临床研究分析发现颈动脉 IMT 每增加 0.1 mm, 发生心肌梗死的风险增加 10%~15%, 并认为颈动脉 IMT 可以预测冠心病发病风险。Osawa K 等^[20]也报道颈动脉 IMT>1.15 mm 者发生冠心病风险为 94%。本研究结果显示 ACS 组颈动脉 IMT 显著高于 SAP 组和对照组, SAP 组颈动脉 IMT 显著高于对照组, 表明冠心病患者颈动脉 IMT 显著升高, 且 ACS 患者颈动脉 IMT 显著高于 SAP 患者。提示颈动脉 IMT 可以反映冠状动脉病变情况。进一步分析显示随着冠状动脉病变血管支数的增加、病变程度的加重, 颈动脉 IMT 逐渐增加, 提示颈动脉 IMT 可以作为评估冠状动脉病变的指标。

H-FABP 是由 134 个氨基酸组成的小分子可溶性蛋白, 主要存在于心肌细胞浆内, 占心脏全部可溶性蛋白的 4~8%^[21,22]。H-FABP 是心肌细胞内脂肪酸代谢和运输的重要载体, 它可以结合并运输长链脂肪酸, 实现心肌能量的供应, 同时起到调节心肌脂肪酸代谢的作用^[23]。研究表明^[24,25], 当心肌细胞受损时, 心肌可以大量动员脂肪酸以提供能量, 导致受损心肌细胞内 H-FABP 迅速升高, 并引起外周血 H-FABP 水平迅速升高。Turan T 等报道^[26]显示, 在 ACS 早期诊断中 H-FABP 与 cTnI 相当, 诊断效率优于 CK-MB。黄赞鸿等报道^[27]显示在近期发作的 ACS 患者中血清 H-FABP 水平与患者心肌损伤数量呈正相关。本研究结果显示 ACS 组血清 H-FABP 水平显著高于 SAP 组和对照组, 表明冠心病患者血清 H-FABP 显著升高。进一步分析显示, 随着病变程度的加重, 血清 H-FABP 逐渐升高, 提示血清 H-FABP 可以作为评估冠状动脉病变的指标。我们也注意到多支病变组和双支病变组血清 H-FABP 水平比较无统计学意义。分析其原因可能与以下几方面有关: (1) H-FABP 主要与心肌受损情况有关, 冠状动脉血管病变支数可能与心肌受损情况不一致, 导致多支病变组和双支病变组血清 H-FABP 水平比较无统计学意义; (2) H-FABP 在心肌损伤后 1.5~3h 内升高, 6~8h 达到高峰^[28-30], 因此在急、慢性心脏病中血清 H-FABP 水平可能存在差异, 而冠状动脉血管病变支数可能与急、慢性心脏病发生并不一致, 导致多支病变组和双支病变组血清 H-FABP 水平比较无统计学意义。介于本次研究样本量偏少, 以后可继续增加样本量进一步研究证实。本研究还发现, 冠心病患者血清 H-FABP 水平与颈动脉 IMT 呈正相关。由于冠心病是一种多因素的疾病, 涉及多种危险因素, 而 H-FABP 和颈动脉 IMT 的异常改变均与动脉粥样硬化的发生、发展有关系, 两者在反映冠状动脉病变程度上具有一致性, 都与冠心病有着密不可分的联系。

综上所述, 冠心病患者血清 H-FABP 水平与颈动脉 IMT 异常升高, 且两者呈正相关, 提示通过对血清 H-FABP 水平与颈动脉 IMT 联合检测可以为冠心病的诊断提供依据。

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