

血清超敏 C 反应蛋白、白介素 6、肿瘤坏死因子 α 水平与持续性心房颤动并肺部感染患者左心房结构改变的关系研究

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【摘要】 目的 分析血清超敏 C 反应蛋白 (hs-CRP)、白介素 6 (IL-6)、肿瘤坏死因子 α (TNF- α) 水平与持续性心房颤动并肺部感染患者左心房结构改变的关系。方法 选取 2014 年 6 月—2015 年 6 月成都市郫县中医医院内一科收治的持续性心房颤动患者 150 例作为房颤组, 根据有无肺部感染分为肺部感染组 54 例, 无肺部感染组 96 例; 根据左心房内径 (LAD) 分为 LAD > 40 mm 组 92 例和 LAD \leq 40 mm 组 58 例。选取同期在本院门诊体检的窦性心律者 50 例作为对照组。比较对照组与观察组受试者血清 hs-CRP、IL-6、TNF- α 水平及左心房结构指标 [LAD、左心房后壁背向散射积分 (IBS) 及背向散射积分周期变化值 (CVIB)], 比较肺部感染组与无肺部感染组患者血清 hs-CRP、IL-6、TNF- α 水平及左心房结构指标, 比较 LAD > 40 mm 组与 LAD \leq 40 mm 组患者血清 hs-CRP、IL-6、TNF- α 水平。结果 房颤组患者血清 hs-CRP、IL-6、TNF- α 水平及 IBS 高于对照组, LAD 大于对照组, CVIB 低于对照组 ($P < 0.05$)。肺部感染组患者血清 hs-CRP、IL-6、TNF- α 水平高于无肺部感染组 ($P < 0.05$); 两组患者 LAD、IBS、CVIB 比较, 差异无统计学意义 ($P > 0.05$)。LAD > 40 mm 组患者血清 hs-CRP、IL-6、TNF- α 水平高于 LAD \leq 40 mm 组 ($P < 0.05$)。结论 持续性心房颤动并肺部感染患者血清 hs-CRP、IL-6、TNF- α 水平升高, 左心房增大并伴有心肌纤维化, hs-CRP、IL-6、TNF- α 可能参与左心房结构改变过程。

【关键词】 心房颤动; 肺部感染; 炎性因子; 左心房

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Correlations between Serum Levels of hs-CRP, IL-6 and TNF- α and Left Atrium Structure Change of Persistent Atrial Fibrillation Patients Complicated with Pulmonary Infection TANG Jian-qin. The First Department of Internal Medicine, the Traditional Chinese Medicine Hospital of Pi County, Chengdu, Chengdu 611730, China

【Abstract】 **Objective** To analyze the correlations between serum levels of hs-CRP, IL-6 and TNF- α and left atrium structure change of persistent atrial fibrillation patients complicated with pulmonary infection. **Methods** From June 2014 to June 2015, a total of 150 patients with persistent atrial fibrillation were selected as case group in the First Department of Internal Medicine, the Traditional Chinese Medicine Hospital of Pi County, Chengdu, and they were divided into A1 group (complicated with pulmonary infection, $n = 54$) and A2 group (did not complicate with pulmonary infection, $n = 96$) according to the incidence of pulmonary infection, into B1 group (with LAD over 40 mm) and B2 group (with LAD equal or less than 40 mm) according to the LAD; and a total of 50 people with sinus rhythm who admitted to this hospital for physical examination were selected as control group at the same time. Serum levels of hs-CRP, IL-6 and TNF- α and left atrial structural parameters [including LAD, integrated backscatter of left atrium posterior wall (IBS) and periodic change value of integrated backscatter (CVIB)] were compared between control group and case group, between A1 group and A2 group; meanwhile serum levels of hs-CRP, IL-6 and TNF- α were compared between B1 group and B2 group. **Results** Serum levels of hs-CRP, IL-6 and TNF- α , and IBS of case group were statistically significantly higher than those of control group, LAD of case group was statistically significantly larger than that of control group, while CVIB of case group was statistically significantly lower than that of

control group ($P < 0.05$). Serum levels of hs-CRP, IL-6 and TNF- α of A1 group were statistically significantly higher than those of control group ($P < 0.05$); no statistically significant differences of LAD, IBS or CVIB was found between A1 group and A2 group ($P > 0.05$). Serum levels of hs-CRP, IL-6 and TNF- α of B1 group were statistically significantly higher than those of B2 group ($P < 0.05$). **Conclusion** Serum levels of hs-CRP, IL-6 and TNF- α of persistent atrial fibrillation patients complicated with pulmonary infection are significantly elevated, existing left atrial enlargement and myocardial fibrosis, hs-CRP, IL-6 and TNF- α may play important roles in the change of left atrium structure.

[Key words] Atrial fibrillation; Pulmonary infection; Inflammatory factor; Left atrium

心房颤动 (atrial fibrillation) 是心律失常的常见类型之一, 老年人多发病及常见病, 随着年龄增长其发病率呈升高趋势。冠心病是引发心房颤动的最常见疾病^[1-2], 部分冠心病患者甚至出现持续性心房颤动, 同时易并发肺部感染^[3-4]。临床研究显示, 炎性因子所致的炎性反应可能参与心房颤动的发生过程, 且肺部感染患者多种血清炎性因子水平出现异常升高^[5-8]。本研究旨在分析血清超敏 C 反应蛋白 (hs-CRP)、白介素 6 (IL-6)、肿瘤坏死因子 α (TNF- α) 水平与持续性心房颤动并肺部感染患者左心房结构改变的关系, 并试着阐述炎性因子在持续性心房颤动并肺部感染患者左心房结构改变中的作用机制。

1 资料与方法

1.1 一般资料 选取 2014 年 6 月—2015 年 6 月成都市郫县中医医院内一科收治的持续性心房颤动患者 150 例作为房颤组, 根据有无肺部感染分为肺部感染组 54 例, 无肺部感染组 96 例; 根据左心房内径 (LAD) 分为 LAD > 40 mm 组 92 例和 LAD \leq 40 mm 组 58 例。纳入标准: (1) 结合病史及心电图检查等确诊为心房颤动, 持续时间 > 7 d, 符合持续性心房颤动诊断标准; (2) 在纳入研究前未进行系统治疗; (3) 停用抗心律失常药物超过 2 个 $t_{1/2}$ 。排除标准: (1) 合并除肺部感染之外其他急慢性感染性疾病者; (2) 急性心肌炎等可逆性病因所致心房颤动者; (3) 有心脏手术史者; (4) 其他疾病终末期者; (5) 近 1 个月内有免疫抑制剂等抗炎药物治疗史者; (6) 合并恶性肿瘤、免疫系统疾病及组织损伤性疾病者。选取同期在本院门诊体检的窦性心律者 50 例作为对照组, 排除标准同房颤组。两组受试者性别、年龄、基础疾病及吸烟史阳性率比较, 差异均无统计学意义 ($P > 0.05$, 见表 1), 具有可比性。

1.2 方法

1.2.1 hs-CRP、IL-6、TNF- α 检测方法 房颤组患者入院后第 1 天、对照组受试者体检当天均抽取空腹外周静脉血 5 ml, 静置 4 h 后 3 000 r/min 离心 30 min, 留取血清。采用免疫比浊法检测血清 hs-CRP 水平, 采用双抗体酶联免疫吸附法检测血清 IL-6、TNF- α 水平, 试剂盒均购自深圳晶美生物科技公司。

1.2.2 左心房结构指标测定方法 采用 HP5500 彩色多

普勒超声诊断仪 (飞利浦公司生产) 测定两组受试者 LAD, 探头频率为 2 ~ 4 MHz; 测定左心房后壁背向散射积分 (IBS) 及背向散射积分周期变化值 (CVIB)。

1.3 观察指标 比较对照组与房颤组受试者血清 hs-CRP、IL-6、TNF- α 水平及左心房结构指标 (LAD、IBS、CVIB), 比较肺部感染组与无肺部感染组患者血清 hs-CRP、IL-6、TNF- α 水平及左心房结构指标, 比较 LAD > 40 mm 组与 LAD \leq 40 mm 组患者血清 hs-CRP、IL-6、TNF- α 水平。

1.4 统计学方法 采用 SPSS 19.0 统计学软件进行数据处理, 计量资料以 ($\bar{x} \pm s$) 表示, 采用两独立样本 t 检验; 计数资料采用 χ^2 检验。以 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 对照组与房颤组受试者血清 hs-CRP、IL-6、TNF- α 水平及左心房结构指标比较 房颤组患者血清 hs-CRP、IL-6、TNF- α 水平及 IBS 高于对照组, LAD 大于对照组, CVIB 低于对照组, 差异有统计学意义 ($P < 0.05$, 见表 2)。

2.2 肺部感染组与无肺部感染组患者血清 hs-CRP、IL-6、TNF- α 水平及左心房结构指标比较 肺部感染组患者血清 hs-CRP、IL-6、TNF- α 水平高于无肺部感染组, 差异有统计学意义 ($P < 0.05$); 两组患者 LAD、IBS、CVIB 比较, 差异无统计学意义 ($P > 0.05$, 见表 3)。

2.3 LAD > 40 mm 组与 LAD \leq 40 mm 组患者血清 hs-CRP、IL-6、TNF- α 水平比较 LAD > 40 mm 组患者血清 hs-CRP、IL-6、TNF- α 水平高于 LAD \leq 40 mm 组, 差异有统计学意义 ($P < 0.05$, 见表 4)。

表 4 LAD > 40 mm 组与 LAD \leq 40 mm 组患者血清 hs-CRP、IL-6、TNF- α 水平比较 ($\bar{x} \pm s$)

Table 4 Comparison of serum levels of hs-CRP, IL-6, TNF- α of persistent atrial fibrillation patients with LAD over 40 mm or not

组别	例数	hs-CRP (mg/L)	IL-6 (ng/L)	TNF- α (ng/L)
LAD > 40 mm 组	92	7.21 \pm 1.41	156.23 \pm 44.15	135.32 \pm 42.11
LAD \leq 40 mm 组	58	6.23 \pm 1.04	125.43 \pm 36.50	111.21 \pm 32.32
t 值		4.89	4.64	3.95
P 值		< 0.05	< 0.05	< 0.05

表 1 对照组与房颤组受试者一般资料比较 [n (%)]

Table 1 Comparison of general information between control group and case group

组别	例数	性别		年龄(岁)		基础疾病		吸烟史
		男	女	<60	≥60	高血压	糖尿病	
对照组	50	28(58.0)	22(42.0)	13(26.0)	37(74.0)	10(20.0)	3(6.0)	11(22.0)
房颤组	150	82(54.7)	68(45.3)	43(28.7)	107(71.3)	34(22.7)	12(8.0)	47(31.3)
χ^2 值		0.03		0.13		0.16	0.02	1.59
P 值		>0.05		>0.05		>0.05	>0.05	>0.05

表 2 对照组与房颤组受试者血清hs-CRP、IL-6、TNF- α 水平及左心房结构指标比较 ($\bar{x} \pm s$)

Table 2 Comparison of serum levels of hs-CRP, IL-6, TNF- α , and left atrial structural parameters between control group and case group

组别	例数	hs-CRP(mg/L)	IL-6(ng/L)	TNF- α (ng/L)	LAD(mm)	IBS(%)	CVIB
对照组	50	0.51 \pm 0.32	21.94 \pm 3.40	14.06 \pm 2.23	28.12 \pm 3.01	31.21 \pm 5.67	8.33 \pm 1.40
房颤组	150	6.92 \pm 1.39	143.95 \pm 43.89	114.57 \pm 42.13	44.92 \pm 2.13	43.93 \pm 6.40	6.55 \pm 1.82
t 值		32.27	19.60	16.83	43.26	12.50	6.32
P 值		<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

注: hs-CRP = 超敏 C 反应蛋白, IL-6 = 白介素 6, TNF- α = 肿瘤坏死因子 α , LAD = 左心房内径, IBS = 背向散射积分, CVIB = 背向散射积分周期变化值

表 3 肺部感染组与无肺部感染组患者血清hs-CRP、IL-6、TNF- α 水平及左心房结构指标比较 ($\bar{x} \pm s$)

Table 3 Comparison of serum levels of hs-CRP, IL-6, TNF- α , and left atrial structural parameters of persistent atrial fibrillation patients complicated with pulmonary infection or not

组别	例数	hs-CRP(mg/L)	IL-6(ng/L)	TNF- α (ng/L)	LAD(mm)	IBS(%)	CVIB
肺部感染组	54	7.39 \pm 1.45	161.12 \pm 45.11	136.11 \pm 43.72	45.02 \pm 2.12	44.06 \pm 6.41	6.60 \pm 1.85
无肺部感染组	96	6.12 \pm 1.22	121.12 \pm 34.54	101.05 \pm 36.26	44.89 \pm 2.10	43.87 \pm 6.34	6.34 \pm 1.77
t 值		14.71	6.08	5.27	0.36	0.18	0.85
P 值		<0.05	<0.05	<0.05	>0.05	>0.05	>0.05

3 讨论

血清及血浆中炎症反应标志物一般分为 3 类, 包括急性时相蛋白、可溶性黏附因子和细胞因子, IL-6 和 TNF- α 属于细胞因子, 主要由单核细胞产生; hs-CRP 属于急性时相蛋白, 是非特异性炎症标志物, 主要由肝细胞合成, 由 IL-6 诱导产生, 且其在机体炎症初期即可在血液中检测到^[9]。IL-6 的主要功能是调节机体免疫及代谢过程, 其是多种病理过程中的主要递质, 同时还可诱导 TNF- α 产生。LAD、IBS、CVIB 均是与左心房结构变化相关的指标, LAD 增大提示左心房增大, IBS 和 CVIB 的变化主要与心肌胶原含量及心肌纤维化程度有关, 当心肌出现胶原沉积及纤维化时会导致 IBS 升高及 CVIB 降低。

临床研究显示, 心房颤动是心肌退化和纤维化的结果^[5-7], 且炎症反应可参与心房颤动的整个发病过程。冠心病的病理基础是冠状动脉粥样硬化, 而在动脉粥样硬化斑块中一直存在无菌性炎症反应, 可表现为 hs-CRP、IL-6、TNF- α 等炎症因子异常表达^[10-12]。肺部感染以细菌感染多见, 肺组织中大量中性粒细胞、单核巨噬细胞浸润可引起局部炎症因子大量释放, 从而激活补体系统及免疫过程。心房颤动和肺部感染均可导致炎症因子异常表达, 但炎症反应是否对心房颤动并肺部感染患者左心房结构产生影响目前研究报道较少。本研究

结果显示, 房颤组患者血清 hs-CRP、IL-6、TNF- α 水平及 IBS 高于对照组, LAD 大于对照组, CVIB 低于对照组, 提示心房颤动患者存在炎症反应、左心房增大、心肌纤维化等; 亚组分析结果显示, 肺部感染组患者血清 hs-CRP、IL-6、TNF- α 水平高于无肺部感染组, 两组患者 LAD、IBS、CVIB 间无差异, 提示合并肺部感染的心房颤动患者机体内炎症反应过程可表现为急性反应, 但肺部感染对左心房结构无影响, 提示长期慢性炎症反应可能对左心房结构产生影响, 但急性炎症反应对左心房结构影响轻微; 进一步比较 LAD > 40 mm 组与 LAD \leq 40 mm 组患者血清炎症因子水平发现, LAD > 40 mm 组患者血清 hs-CRP、IL-6、TNF- α 水平高于 LAD \leq 40 mm 组, 推测炎症反应可能参与持续性心房颤动并肺部感染患者左心房结构改变过程。

综上所述, 持续性心房颤动并肺部感染患者血清 hs-CRP、IL-6、TNF- α 水平升高, 左心房增大并伴有心肌纤维化, hs-CRP、IL-6、TNF- α 可能参与左心房结构改变过程。

本文无利益冲突。

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