

· 临床研究 ·

老年高血压患者左心室肥厚与动态血压参数和炎症标志物的相关性

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【摘要】目的 探讨老年高血压患者合并左心室肥厚(LVH)与动态血压(ABPM)参数和常见的心血管炎症因子水平的相关性。**方法** 筛选2012年1月至2013年12月于解放军总医院干部诊疗科门诊就诊的患者, 纳入符合入选标准的初次诊断为高血压的患者152例, 其中单纯高血压109例, 合并LVH 43例。全部患者接受ABPM检查, 测定血清高敏C反应蛋白(hs-CRP)和同型半胱氨酸(Hcy)水平。分析ABPM参数与hs-CRP和Hcy水平的相关性。**结果** 老年高血压合并LVH组24h平均收缩压(24hSBP)、夜间平均收缩压(nSBP)和夜间平均脉压(nPP)均显著高于单纯老年高血压患者($P < 0.05$, $P < 0.01$); 同时, 合并LVH患者中血清hs-CRP水平显著高于单纯高血压患者($P < 0.05$), 而血清Hcy在两组患者间差异无统计学意义($P > 0.05$)。logistic回归分析显示, nSBP和hs-CRP水平与高血压患者合并LVH相关。**结论** 老年高血压患者nSBP增高和hs-CRP水平升高与合并LVH风险增高相关。

【关键词】 老年人; 高血压; 左心室肥厚; 高敏C反应蛋白; 同型半胱氨酸

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Correlation of ambulatory blood pressure monitoring parameters and inflammatory biomarker levels with left ventricular hypertrophy in elderly hypertensive patients

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【Abstract】Objective To investigate the correlation of left ventricular hypertrophy (LVH) with parameters of ambulatory blood pressure monitoring (ABPM) and the levels of established inflammatory biomarkers in the elderly with hypertension. **Methods** Totally 152 elderly patients with newly-diagnosed hypertension who were screened from the consecutive patients in Out-patient Department of Chinese PLA General Hospital from January 2012 to December 2013 were enrolled in this study. There were 43 patients combined with LVH and 109 without. ABPM was performed in all subjects. Blood levels of high sensitivity C-reactive protein (hs-CRP) and homocysteine (Hcy) were measured. The correlation of the parameters and the levels with LVH was analyzed. **Results** In the ABPM parameters, the 24 hours mean systolic blood pressure (24hSBP), nighttime mean systolic blood pressure (nSBP) and nighttime mean pulse pressure (nPP) were significantly higher in the patients with LVH than in those without ($P < 0.05$, $P < 0.01$). The serum level of hs-CRP was also obviously higher in those with LVH ($P < 0.05$), but no such difference was found in the level of Hcy between the 2 groups ($P > 0.05$). Logistic regression analysis showed that nSBP and hs-CRP level were correlated with LVH in the hypertensive patients. **Conclusion** Elevated nSBP and higher hs-CRP level increase the risk of LVH in the elderly hypertensive patients.

【Key words】 elderly; hypertension; left ventricular hypertrophy; high sensitivity C-reactive protein; homocysteine

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左心室肥厚(left ventricular hypertrophy, LVH)是高血压常见的并发症,也是高血压患者心血管事件的独立危险因素,而老年患者更是LVH的高发人群^[1,2]。研究显示血压升高相关的机械刺激是导致

LVH的重要因素之一;而另一重要因素为神经内分泌的激活而引发的炎症反应^[3],而高敏C反应蛋白(high sensitivity C-reactive protein, hs-CRP)^[4,5]与同型半胱氨酸(homocysteine, Hcy)均为高血

压患者与预后相关的炎症因子^[6,7]。本研究旨在分析老年高血压患者LVH与各动态血压(ambulatory blood pressure monitoring, ABPM)参数、hs-CRP和Hcy的关系。

1 对象与方法

1.1 研究对象

筛查2012年1月至2013年12月于解放军总医院干部诊疗科门诊就诊的患者。纳入初次诊断的原发性高血压患者,高血压诊断依据《中国高血压防治指南(第3版)》(2010年修订版),即非同日3次收缩压 ≥ 140 mmHg(1mmHg = 0.133kPa)和(或)舒张压 ≥ 90 mmHg;并排除具有如下任一情况患者:继发性高血压,糖尿病,冠心病、瓣膜性心脏病、先天性心脏病和其他器质性心脏病,恶性肿瘤,免疫系统疾病,以及肝肾功能异常。最终入组老年高血压患者152例,其中男性89例、女性63例,年龄61~74岁。根据心脏超声检查将患者分为单纯高血压组(109例)和高血压合并LVH组(43例)。心脏超声检查采用飞利浦IE-33彩色多普勒超声诊断仪,探头频率2.2~4.0MHz,采用Devereux公式计算左心室质量指数(left ventricular mass index, LVMI);LVH的诊断标准:男性LVMI > 125 g/m²,女性LVMI > 120 g/m²。

1.2 临床资料采集和炎症因子测定

测量身高、体质量,计算体质量指数(body mass index, BMI)。采集晨间空腹肘静脉血5ml,3000转/min离心分离血清,测定空腹血糖(fasting plasma glucose, FPG)、甘油三酯(triglycerides, TG)、总胆固醇(total cholesterol, TC)、高密度脂蛋白胆固醇(high density lipoprotein cholesterol, HDL-C)、低密度脂蛋白胆固醇(low density lipoprotein cholesterol, LDL-C)、血肌酐(serum creatinine, SCr)和血尿酸(uric acid, UA);同时采用免疫比浊法测定hs-CRP,酶免疫法测定Hcy。上述生化测定均使用日立7600型全自动生化分析仪及相应试剂盒。

1.3 动态血压监测

采用日本产TM2421型动态血压监测仪,袖带绑缚于非优势臂,设定日间(8:00~22:00)每30min、夜间(22:00~8:00)每60min自动充气记录血压1次,监测时间为8:00~次日8:00。计算机自动计算24h平均收缩压(24h mean systolic blood pressure, 24hSBP)、日间平均收缩压(daytime mean systolic

blood pressure, dSBP)和夜间平均收缩压(nighttime mean systolic blood pressure, nSBP)、24h平均舒张压(24h mean diastolic blood pressure, 24hDBP)、日间平均舒张压(daytime mean diastolic blood pressure, dDBP)和夜间平均舒张压(nighttime mean diastolic blood pressure, nDBP)、24h平均脉压(24h mean pulse pressure, 24hPP)、日间平均脉压(daytime mean pulse pressure, dPP)和夜间平均脉压(nighttime mean pulse pressure, nPP)。

1.4 统计学处理

采用SPSS19.0统计软件进行统计分析。计量资料以均数 $\pm$ 标准差($\bar{x} \pm s$)或中位数(M)表示,计量资料组间比较采用 t 检验(方差齐)或 t' 检验(方差不齐),其中血清hs-CRP和Hcy水平呈正偏态分布,对两者进行对数转换后检验其分布近似正态后采用 t 检验。计数资料用百分率表示,组间比较采用 χ^2 检验。多因素分析采用logistic回归分析。 $P < 0.05$ 为差异具有统计学意义。

2 结果

2.1 两组患者基本临床特征比较

单纯高血压患者与高血压合并LVH患者在年龄、性别组成上差异均无统计学意义($P > 0.05$),两组的一般代谢参数BMI、FPG、TC、TG、HDL-C、LDL-C、SCr和UA差异也无统计学意义($P > 0.05$;表1)。

表1 两组患者的基本临床特征
Table 1 Clinical characteristics of the two groups

Item	Hypertension without LVH group (n = 109)	Hypertension with LVH group (n = 43)
Age(years, $\bar{x} \pm s$)	67.98 $\pm$ 6.79	69.07 $\pm$ 7.51
Male[n(%)]	64 (58.72)	19 (55.81)
BMI(kg/m ² , $\bar{x} \pm s$)	23.15 $\pm$ 3.21	24.08 $\pm$ 4.71
FPG(mmol/L, $\bar{x} \pm s$)	5.54 $\pm$ 1.05	5.83 $\pm$ 1.13
TC(mmol/L, $\bar{x} \pm s$)	5.19 $\pm$ 1.25	5.32 $\pm$ 1.45
TG(mmol/L, $\bar{x} \pm s$)	1.72 $\pm$ 1.09	1.95 $\pm$ 1.18
HDL-C(mmol/L, $\bar{x} \pm s$)	1.31 $\pm$ 0.39	1.25 $\pm$ 0.41
LDL-C(mmol/L, $\bar{x} \pm s$)	3.42 $\pm$ 0.75	3.53 $\pm$ 0.82
SCr(μ mol/L, $\bar{x} \pm s$)	78.34 $\pm$ 13.87	80.25 $\pm$ 16.87
UA(μ mol/L, $\bar{x} \pm s$)	305.05 $\pm$ 82.01	319.08 $\pm$ 79.41

LVH: left ventricular hypertrophy; BMI: body mass index; FPG: fasting plasma glucose; TC: total cholesterol; TG: triglycerides; HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol; SCr: serum creatinine; UA: uric acid

2.2 两组患者炎症因子水平比较

单纯高血压患者hs-CRP水平显著低于合并LVH

患者 ($P < 0.05$) ; 同时, 单纯高血压患者Hcy水平与合并LVH患者相比差异无统计学意义 ($P > 0.05$; 表2)。

表2 两组患者的hs-CRP和Hcy水平
Table 2 Levels of hs-CRP and Hcy in the two groups

Index	Hypertension without LVH group (n = 109)	Hypertension with LVH group (n = 43)
hs-CRP(mg/L, M)	0.94	4.14
lg hs-CRP ($\bar{x} \pm s$)	-0.03 ± 0.15	$0.61 \pm 0.11^*$
Hcy($\mu\text{mol/L}$, M)	16.83	20.51
lg Hcy ($\bar{x} \pm s$)	1.21 ± 0.83	1.29 ± 0.85

LVH: left ventricular hypertrophy; hs-CRP: high sensitivity C-reactive protein; Hcy: homocysteine. Compared with hypertension without LVH group, $^*P < 0.05$

2.3 动态血压参数

高血压合并LVH患者的24hSBP ($P < 0.05$)、nSBP ($P < 0.01$) 和nPP ($P < 0.01$) 均显著高于单纯高血压患者, 而两组患者的dSBP、24hDBP、dDBP、nDBP、24hPP和dPP差异均无统计学意义 ($P > 0.05$; 表3)。

表3 两组患者的动态血压参数比较
Table 3 Comparison of ABPM data between the two groups (mmHg, $\bar{x} \pm s$)

Parameter	Hypertension without LVH group (n = 109)	Hypertension with LVH group (n = 43)
24hSBP	144.63 ± 10.19	$149.46 \pm 12.48^*$
dSBP	147.84 ± 11.43	150.82 ± 13.85
nSBP	135.21 ± 10.62	$144.02 \pm 12.91^{**}$
24hDBP	81.57 ± 10.06	83.34 ± 10.54
dDBP	83.14 ± 10.79	85.28 ± 11.55
nDBP	79.29 ± 9.11	81.86 ± 10.95
24hPP	60.45 ± 8.93	63.04 ± 7.75
dPP	63.21 ± 8.74	65.02 ± 9.63
nPP	57.93 ± 6.89	$62.36 \pm 9.18^{**}$

ABPM: ambulatory blood pressure monitoring; LVH: left ventricular hypertrophy; 24hSBP: 24h mean systolic blood pressure; dSBP: daytime mean systolic blood pressure; nSBP: nighttime mean systolic blood pressure; 24hDBP: 24h mean diastolic blood pressure; dDBP: daytime mean diastolic blood pressure; nDBP: nighttime mean diastolic blood pressure; 24hPP: 24h mean pulse pressure; dPP: daytime mean pulse pressure; nPP: nighttime mean pulse pressure. 1mmHg = 0.133kPa. Compared with hypertension without LVH group, $^*P < 0.05$, $^{**}P < 0.01$

2.4 合并LVH的logistic相关性分析

以LVH为因变量, logistic相关分析纳入hs-CRP、24hSBP、nSBP、nPP, 结果显示本组队列中hs-CRP ($P = 0.0214$; OR = 1.21, 95%CI 1.09~1.32)和nSBP ($P = 0.0013$; OR = 1.07, 95%CI 1.05~1.09) 与合并LVH独立相关。

3 讨论

国内外许多研究证实, 年龄、性别、血压、血

糖、胰岛素以及肥胖是LVH的独立危险因素^[8-10]。其中血压是一项重要的可控危险因素, 控制血压是高血压患者预防包括LVH在内的靶器官损害的首要目标。与传统的单次血压测定参数相比, ABPM具有数据更完整和全面的优势, 近年来随着ABPM的普及而被更多地应用于相关研究。

研究显示, 日间血压和夜间血压都是LVH的独立危险因素。与舒张压相比, 收缩压(日间和夜间)与LVH的关系更密切^[11]。大型高血压干预研究LIFE也证实有效控制24hSBP可延缓或逆转高血压患者LVH^[12]。Framingham研究甚至显示, 脉压对心血管风险的预测性甚至高于收缩压、舒张压^[13]。本研究结果显示, 合并LVH的患者24hSBP、nSBP和nPP均更高, 且回归分析证实nSBP是LVH的独立危险因素。nSBP的重要性与上述研究一致。

除机械刺激外, LVH的另一个重要的发生机制即心脏局部因神经内分泌系统激活而引发的慢性炎症反应^[3]。hs-CRP是一项目前广受重视的预测心血管风险的炎症指标。流行病学研究显示, hs-CRP水平与心血管疾病风险独立相关, hs-CRP $> 3\text{mg/L}$ 可视为心血管疾病风险增加。高血压患者中hs-CRP水平升高, 且与血压相关^[4]。基础研究显示, 血压升高可触发血管内皮细胞的促炎症反应, 而导致分泌增加, hs-CRP可在病变局部沉积, 诱发内皮细胞表达和分泌黏附分子和化学趋化因子、促进巨噬细胞对LDL的摄取、促进其他细胞因子分泌、增强局部纤溶活性、扩大其他炎性介质的促炎症效应^[14]。与上述研究结果一致, 本研究显示, 高血压合并LVH患者中hs-CRP水平高于单纯高血压患者, 且与LVH独立相关。进一步支持LVH患者中确实存在炎症反应的激活。

Hcy是另一项广受关注的心血管风险的炎症预测指标。Hcy为一种含硫氨基酸, 是甲硫氨酸(蛋氨酸)代谢的重要中间产物。近年来国内外均有大量研究表明, 高Hcy血症与冠心病、脑卒中等大血管病变相关, 血Hcy水平升高是动脉粥样硬化的一个独立危险因素^[7]。中国高血压指南已推荐Hcy $\geq 10\mu\text{mol/L}$ 为高血压患者分层的危险因素。一项我国6大城市的研究数据显示, 我国成年高血压患者中约75%合并Hcy升高^[15]。研究显示, Hcy可通过促进氧化反应加重高血压引起心肌肥厚和心肌纤维化, 可引起线粒体通透性改变, 使心肌细胞收缩功能异常, 还可通过激活交感神经系统, 导致心肌肥厚^[16]。本研究并未发现合并LVH患者Hcy水平高于单纯高血压患者。鉴于本研究队列样本量较少,

因此并不能证实Hcy水平与LVH不相关。本研究队列也未检出其他几项众所周知的LVH危险因素,包括年龄、性别、肥胖、血糖以及除nSBP外的其他动态血压参数,可能也与样本量偏小有关。

总之,本研究在初诊未治的老年高血压队列中评估影响LVH的危险因素,因入选标准较好地排除了病程、合并疾病、治疗因素对结果的影响,尽管样本量较小,结果仍提示nSBP升高和hs-CRP水平升高与老年高血压合并LVH的危险独立相关。

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