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老年原发性高血压患者血清 SF、hs-CRP、Hcy、Cys C 水平及血脂指标与颈动脉内膜中层厚度的相关性研究 *

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摘要 目的:研究老年原发性高血压(EH)患者血清铁蛋白(SF)、超敏 C 反应蛋白(hs-CRP)、同型半胱氨酸(Hcy)、胱抑素 C(Cys C)水平及血脂指标与颈动脉内膜中层厚度(IMT)的相关性。**方法:**选择从 2016 年 6 月到 2018 年 1 月在广州军区广州总医院心血管内科接受治疗的 100 例老年 EH 患者作为研究对象。根据颈动脉的 IMT 值将患者分为斑块形成组(IMT $\geq$ 1.3 mm)30 例、IMT 增厚组(1.0 mm<IMT<1.3 mm)42 例、IMT 正常组(IMT $\leq$ 1.0 mm)28 例,对比各组血脂指标以及血清 SF、hs-CRP、Hcy、Cys C 水平,分析 IMT 与血脂指标及 SF、hs-CRP、Hcy、Cys C 的相关性,并分析 IMT 增厚的危险因素。**结果:**斑块形成组和 IMT 增厚组的总胆固醇(TC)和低密度脂蛋白胆固醇(LDL-C)水平明显高于 IMT 正常组($P<0.05$),且斑块形成组又高于 IMT 增厚组($P<0.05$)。斑块形成组和 IMT 增厚组的血清 SF、hs-CRP、Hcy 及 Cys C 水平明显高于 IMT 正常组 ($P<0.05$), 且斑块形成组又高于 IMT 增厚组($P<0.05$)。根据 Spearman 相关性分析显示,老年 EH 患者 IMT 与 SF、hs-CRP、Hcy、Cys C、TC 及 LDL-C 均呈正相关($P<0.05$)。根据 Logistic 回归分析结果显示,SF、hs-CRP、Hcy、Cys C 均是老年 EH 患者 IMT 增厚的危险因素($P<0.05$)。**结论:**血脂指标中 TC、LDL-C 及血清 SF、hs-CRP、Hcy、Cys C 水平与老年 EH 患者颈动脉 IMT 密切相关,且 SF、hs-CRP、Hcy、Cys C 是 IMT 增厚的危险因素。

关键词:老年;原发性高血压;铁蛋白;超敏 C 反应蛋白;同型半胱氨酸;胱抑素 C;颈动脉内膜中层厚度

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Correlation Study of Serum SF, hs-CRP, Hcy, and Cys C Levels and Blood Lipid Indexes with Carotid Intima Media Thickness in Elderly Patients with Essential Hypertension*

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ABSTRACT Objective: To investigate the correlation between serum ferritin (SF), high sensitivity C reactive protein (hs-CRP), homocysteine (Hcy) and cystatin C (Cys C) and blood lipid indexes with carotid intima media thickness (IMT) in elderly patients with essential hypertension(EN). **Methods:** 100 elderly patients with EH who were treated in our hospital from June 2016 to March 2018 were selected as the subjects. According to the IMT value of carotid artery, the patients were divided into plaque formation group (IMT $>$ 1.3mm) with 30 cases, IMT thickening group (1.0 mm<IMT<1.3 mm) with 42 cases, IMT normal group (IMT $\leq$ 1.0 mm) with 28 cases. Blood lipid indexes levels, serum SF, hs-CRP, Hcy and Cys C levels in each group were compared. The correlation between IMT and blood lipids indexes, SF, hs-CRP, Hcy and Cys C were analyzed. **Results:** The levels of total cholesterol (TC) and low density lipoprotein cholesterol (LDL-C) in the plaque formation group and the IMT thickening group were significantly higher than those in the IMT normal group, and the plaque formation group was higher than the IMT thickening group ($P<0.05$). The levels of serum SF, hs-CRP, Hcy and Cys C in plaque formation group and IMT thickening group were significantly higher than those in IMT normal group, and plaque formation group was higher than that in IMT thickening group ($P<0.05$). According to Spearman correlation analysis showed that IMT in elderly patients with EH was positively correlated with SF, hs-CRP, Hcy, Cys C, TC and LDL-C ($P<0.05$). According to the result of Logistic regression analysis showed that SF, hs-CRP, Hcy and Cys C were all risk factors for IMT thickening in elderly patients with EH ($P<0.05$). **Conclusion:** The levels of TC, LDL-C and serum SF, hs-CRP, Hcy and Cys C were closely related to the carotid IMT in elderly EH patients, and SF, hs-CRP, Hcy and Cys were the risk factors for IMT thickening.

Key words: Elderly; Essential hypertension; Serum ferritin; High sensitivity C reactive protein; Homocysteine; Cystatin C; Carotid intima-media thickness

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前言

原发性高血压(essential hypertension, EH)多发生于中老年人群,而在我国老年人中的发病率甚至高达 40%,而且发病率具有逐年上升的趋势^[1,2]。此病属于一种慢性疾病,其本身对患者并无十分严重的危害,但由其引发的脑梗死等严重并发症若未给予及时有效的治疗,则可能导致患者残疾或死亡^[3,4]。动脉粥样硬化是多种心血管疾病的病理基础,其可使斑块破裂并形成血栓,颈动脉内膜中层厚度(intima media thickness, IMT)的增大是导致大动脉发生粥样硬化的重要标志^[6,7],并且有报道指出,老年 EH 患者的发病还可能与机体内的微炎症反应等因素有关^[8,9]。因此,本研究通过探讨老年 EH 患者血清学指标水平与颈动脉 IMT 的相关性,旨在为临床诊治 EH 提供相应的参考依据,现报道如下。

1 资料和方法

1.1 一般资料

选择从 2016 年 6 月到 2018 年 1 月在广州军区广州总医院心血管内科接受治疗的 100 例老年 EH 患者作为研究对象。纳入标准:(1)符合世界卫生组织关于高血压的诊断标准^[10];(2)年龄 ≥ 60 岁;(3)患者或其家属已经完全知情本次研究,并已签署知情同意书。排除标准:(1)存在感染者;(2)肾功能不全者;(3)继发性高血压者;(4)免疫类疾病或血液疾病者;(5)恶性肿瘤者。根据颈动脉的 IMT 值将患者分为斑块形成组(IMT ≥ 1.3 mm)30 例,男 16 例,女 14 例;年龄 60-82 岁,平均(71.25 $\pm$ 1.46)岁;病程 1-22 年,平均(12.58 $\pm$ 1.03)年。IMT 增厚组(1.0 mm<IMT<1.3 mm)42 例,男 22 例,女 20 例;年龄 61-78 岁,平均(72.18 $\pm$ 1.52)岁;病程 2-19 年,平均(13.09 $\pm$ 1.14)年。IMT 正常组(IMT ≤ 1.0 mm)28 例,男 15 例,女 13 例;年龄 62-79 岁,平均(70.22 $\pm$ 1.21)岁;病程 2-20 年,平均(11.58 $\pm$ 1.08)年。各组以上资料比较差异无统计学意义($P>0.05$),均衡可比。此次研究已通过广州军区广州总医院伦理委

员会评审和批准。

1.2 方法

1.2.1 各项生化指标的检测 所有患者在入组后抽取其晨间空腹静脉血 4 mL,给予 15 min 3000 r/min 的离心之后分离出血清,通过 MODULAR P800 型全自动生化分析仪(罗氏公司)检测同型半胱氨酸(homocysteine, Hcy)、铁蛋白(serum ferritin, SF)、超敏 C 反应蛋白(high sensitivity C reactive protein, hs-CRP)及胱抑素 C(cystatin C, Cys C)水平,其中 SF 通过电化学发光免疫法测定,Hcy、hs-CRP 及 Cys C 通过免疫比浊法测定。另使用全自动生化分析仪(罗氏公司, Cobas8000 c701 型)检测总胆固醇(TC)、甘油三酯(TG)、高密度脂蛋白胆固醇(HDL-C)和低密度脂蛋白胆固醇(LDL-C)水平,有关试剂盒均购自上海科华生物工程股份有限公司,操作时严格遵守说明书的步骤进行。

1.2.2 颈动脉 IMT 的检测 患者取仰卧位,将颈部暴露出来,通过 AUCUSONS 2000 型彩超仪(西门子公司)对颈动脉 IMT 实施检测,设置探头频率为 10 MHz,由经验丰富的超声诊断医师进行诊断,每位患者均取 3 个诊断周期,将平均值记为颈动脉 IMT 值。

1.3 统计学方法

通过 SPSS21.0 软件进行统计分析,其中 SF、hs-CRP、Hcy 及 Cys C 水平等计量资料以($\bar{x}\pm s$)表示,实施 t 检验,多组间比较采用 F 检验,性别比例等计数资料用[n(%)]表示,实施 χ^2 检验。指标间的相关性采用 Spearman 相关性分析,IMT 增厚的危险因素采用 Logistic 回归分析,检验标准设置为 $\alpha=0.05$ 。

2 结果

2.1 各组血脂指标的对比

各组的 TC 和 LDL-C 水平相比,差异有统计学意义($P<0.05$)。斑块形成组和 IMT 增厚组的 TC 和 LDL-C 水平高于 IMT 正常组,且斑块形成组又高于 IMT 增厚组($P<0.05$)。各组的 TG 和 HDL-C 水平相比,差异无统计学意义($P>0.05$),见表 1。

表 1 各组血脂指标的对比($\bar{x}\pm s$, mmol/L)
Table 1 Comparison of blood lipid indexes of each group($\bar{x}\pm s$, mmol/L)

Groups	n	TC	TG	HDL-C	LDL-C
Plaque formation group	30	5.68 $\pm$ 1.32 ^{*△}	2.44 $\pm$ 0.35	1.21 $\pm$ 0.24	4.02 $\pm$ 0.79 ^{*△}
IMT thickening group	42	4.23 $\pm$ 0.79 [*]	2.45 $\pm$ 0.27	1.23 $\pm$ 0.22	3.61 $\pm$ 0.64 [*]
IMT normal group	28	3.76 $\pm$ 0.51	2.41 $\pm$ 0.26	1.24 $\pm$ 0.20	2.68 $\pm$ 0.40
F	-	4.281	2.017	2.139	3.949
P	-	0.000	0.124	0.089	0.001

Note: Compared with IMT normal group, ^{*} $P<0.05$; compared with IMT thickening group, [△] $P<0.05$.

2.2 各组的血清 SF、hs-CRP、Hcy 及 Cys C 水平对比

各组的血清 SF、hs-CRP、Hcy 及 Cys C 水平相比,差异有统计学意义($P<0.05$)。斑块形成组和 IMT 增厚组的血清 SF、hs-CRP、Hcy 及 Cys C 水平高于 IMT 正常组,且斑块形成组又高于 IMT 增厚组,差异均有统计学意义($P<0.05$),见表 2。

2.3 老年 EH 患者 IMT 与血脂指标及 SF、hs-CRP、Hcy、Cys C

的相关性分析

根据 Spearman 相关性分析显示,老年 EH 患者 IMT 与 SF、hs-CRP、Hcy、Cys C、TC 及 LDL-C 均呈正相关($P<0.05$),而与 TG 和 HDL-C 无明显的相关性($P>0.05$),见表 3。

2.4 IMT 增厚的危险因素分析

以老年 EH 患者 IMT 是否增厚为因变量,以血脂指标及

SF、hs-CRP、Hcy、Cys C 水平为自变量,根据 Logistic 回归分析 险因素($P<0.05$)。
显示,SF、hs-CRP、Hcy、Cys C 均是老年 EH 患者 IMT 增厚的危

表 2 各组的血清 SF、hs-CRP、Hcy 及 Cys C 水平对比($\bar{x}\pm s$)
Table 2 Comparison of serum SF, hs-CRP, Hcy and Cys C levels of each group($\bar{x}\pm s$)

Groups	n	SF(ng/mL)	hs-CRP(mg/L)	Hcy(μ mol/L)	Cys C(mg/L)
Plaque formation group	30	324.87 $\pm$ 83.19* ^a	6.01 $\pm$ 1.37* ^a	26.51 $\pm$ 2.38* ^a	2.57 $\pm$ 0.33* ^a
IMT thickening group	42	196.55 $\pm$ 40.27*	2.89 $\pm$ 0.74*	18.92 $\pm$ 1.47*	1.97 $\pm$ 0.18*
IMT normal group	28	116.30 $\pm$ 21.26	0.83 $\pm$ 0.15	11.23 $\pm$ 1.46	1.03 $\pm$ 0.12
F	-	11.248	4.933	7.215	3.622
P	-	0.000	0.000	0.000	0.001

Note: Compared with IMT normal group,* $P<0.05$; compared with IMT thickening group,^a $P<0.05$.

表 3 老年 EH 患者 IMT 与血脂指标及 SF、hs-CRP、Hcy、Cys C 的相关性分析
Table 3 Correlation analysis of IMT with blood lipid indexes and SF, hs-CRP, Hcy, Cys C in elderly patients with EH

Objects	Statistic value	SF	hs-CRP	Hcy	Cys C	TC	TG	HDL-C	LDL-C
IMT	r	0.582	0.434	0.497	0.510	0.455	0.203	-0.124	0.613
	P	0.002	0.000	0.000	0.000	0.000	0.122	0.157	0.000

表 4 Logistic 回归分析 IMT 增厚的危险因素
Table 4 Logistic regression analysis of risk factors for IMT thickening

Indexes	β	S.E	Wald χ^2	P	OR	95%CI
SF	0.736	0.458	5.039	0.021	2.361	1.157-5.984
hs-CRP	1.289	0.542	5.148	0.028	3.574	1.156-8.681
Hcy	1.052	0.498	3.752	0.042	2.756	1.002-8.238
Cys C	1.412	0.468	6.173	0.011	3.942	1.402-10.985
TC	2.436	0.759	2.143	0.366	1.589	1.033-5.487
HDL-C	3.724	0.752	2.742	0.395	1.568	1.147-8.011

3 讨论

EH 是一种常见的慢性疾病,其对老年人群的健康危害较大,由于患者常常并发急性脑梗死、脑卒中以及急性冠脉综合征等疾病,因此该病的致残率和致死率均较高^[11,12]。据研究证实,动脉粥样硬化通常是上述合并症的发病机制之一^[13,14]。当前临床对于老年 EH 和动脉粥样硬化二者的内在诱因均未完全明确,相关学者认为可能与炎症反应、血管损伤等因素有关^[15,16]。由于 SF、hs-CRP、Hcy、Cys C 及血脂指标均与机体内的炎症存在直接或间接的联系,而 IMT 与动脉粥样硬化密切相关,因此探讨老年 EH 患者血清 SF、hs-CRP、Hcy、Cys C 水平及血脂指标与 IMT 的相关性对于 EH 的临床诊治具有重要意义。

本研究通过分析发现,斑块形成组和 IMT 增厚组的 TC 和 LDL-C 水平高于 IMT 正常组,且斑块形成组又高于 IMT 增厚组($P<0.05$),这提示了 IMT 值较高的老年 EH 患者脂代谢水平异常,可能与患者机体的动脉粥样硬化有关^[17]。具体而言,IMT 值较高的老年 EH 患者通常发生动脉粥样硬化的程度也较大,机体内的血脂水平异常情况较为明显,而 TC 和 LDL-C 均为比较典型的血脂指标,因此 TC、LDL-C 水平在老年 EH 患者中的水平明显升高。同时,斑块形成组和 IMT 增厚组的血清 SF、

hs-CRP、Hcy 及 Cys C 水平高于 IMT 正常组,且斑块形成组又高于 IMT 增厚组($P<0.05$),说明 SF、hs-CRP、Hcy 及 Cys C 可能参与了 EH 的发病过程。SF 属于调控铁代谢的一种关键蛋白,而当血液内铁含量超过常规负荷时能够对机体的 DNA 产生损伤,进而破坏了细胞膜自身的结构和功能,导致血脂代谢紊乱和造成血管内皮细胞的损伤^[18]。hs-CRP 作为一种非特异性炎症因子,其不仅可以促使炎症介质的释放,同时对血管内皮细胞有关黏附因子的表达具有强化作用,从而使血管产生炎症反应,致使内皮组织功能出现紊乱,加速动脉粥样硬化的产生^[19-21]。Hcy 属于蛋氨酸循环性产物,其能够改变机体内凝血因子的功能,并破坏凝血及纤溶之间的平衡,致使血液流变学发生异常,并使血黏度升高^[22,23]。Hcy 还可诱导机体内过氧化物形成,加速血小板的聚集,对血管内皮细胞造成一定的损害^[24,25]。Cys C 属于半胱氨酸有关蛋白酶的抑制剂,其广泛存在于人体体液和各组织的核细胞中,在机体中参与了细胞外基质的降解,对维持血管壁的结构有促进作用^[26,27]。同时,Cys C 能够对 Hcy 分解酶自身的活性产生抑制,并使得 Hcy 水平上升,从而导致血管损伤^[28,29]。当 SF、hs-CRP、Hcy 及 Cys C 水平升高时,引起患者炎症反应和血管损伤,导致机体凝血机制发生变化,进而增加血栓的形成,最终将引发动脉粥样硬化或加速其进

展。此外,本研究根据 Spearman 相关性分析显示,老年 EH 患者 IMT 与 SF、hs-CRP、Hcy、Cys C、TC 及 LDL-C 均呈正相关,可能是因为上述指标均从机体的炎症反应或动脉粥样硬化等方面参与到了 EH 疾病的形成及发展,并对 IMT 的变化产生了一定的影响^[30]。根据 Logistic 回归分析显示,SF、hs-CRP、Hcy、Cys C 均是老年 EH 患者 IMT 增厚的危险因素,说明 SF、hs-CRP、Hcy、Cys C 水平越高,老年 EH 患者 IMT 增厚的几率越大,临床通过检测 SF、hs-CRP、Hcy、Cys C 水平,有助于判断 IMT 增厚情况。

综上所述,老年 EH 患者血脂指标以及血清 SF、hs-CRP、Hcy、Cys C 水平均明显升高,且均与 IMT 均呈正相关,临床上可将上述血清生化指标纳入到诊治老年 EH 患者的指标监测体系,从而更加科学地服务临床诊治过程。

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(上接第 3895 页)

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