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原发性高血压患者动态动脉硬化指数与颈动脉粥样硬化及早期肾损害的相关性研究*

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摘要 目的:探讨原发性高血压(EH)患者动态动脉硬化指数(AASI)与颈动脉粥样硬化及早期肾损害的相关性。**方法:**选取 2017 年 6 月~2018 年 5 月期间我院收治的 147 例 EH 患者记为 EH 组,根据患者颈动脉内中膜厚度(IMT)的不同,将 $IMT \geq 1.0$ mm 的患者记为颈动脉硬化组($n=78$), $IMT < 1.0$ mm 的患者记为无颈动脉硬化组($n=69$);根据患者尿微量白蛋白(MAU)水平的不同,将 MAU 水平为 0~30 mg/24 h 的患者记为 MAU 正常组 ($n=86$),MAU 水平为 30~300 mg/24 h 的患者记为 MAU 升高组($n=61$)。另选取同期于我院进行体检的健康志愿者 60 例记为对照组。比较 EH 组与对照组临床资料,比较 EH 患者中颈动脉硬化组、无颈动脉硬化组的 AASI、颈动脉弹性功能参数,比较 MAU 正常组、MAU 升高组的 AASI、肾功能指标,采用 Pearson 相关性分析分析 EH 患者 AASI 与颈动脉粥样硬化及早期肾损害的相关性。**结果:**EH 组吸烟人数、糖尿病人数、收缩压、舒张压、IMT、AASI、MAU 显著高于对照组($P < 0.05$)。颈动脉硬化组 AASI、血管压力应变弹性系数(Ep)、硬度指数均显著高于无颈动脉硬化组($P < 0.05$),血管顺应性(AC)明显低于无颈动脉硬化组($P < 0.05$)。MAU 升高组 AASI 显著高于 MAU 正常组($P < 0.05$),PRO 显著低于 MAU 正常组($P < 0.05$);而 MAU 升高组与 MAU 正常组肾小球滤过率(GFR)、肌酐清除率(CCr)比较差异无统计学意义($P > 0.05$)。经 Pearson 相关性分析显示,EH 患者中 AASI 与 IMT、MAU、Ep、硬度指数均呈正相关性($P < 0.05$),与 PRO、AC 呈负相关($P < 0.05$),与 GFR、CCr 无相关性($P > 0.05$)。**结论:**EH 患者 AASI 与颈动脉粥样硬化及早期肾损害情况关系密切,临床可通过监测 AASI,以尽早了解患者心血管事件发生风险及靶器官损伤程度。

关键词:原发性高血压;动态动脉硬化指数;颈动脉粥样硬化;肾损害;相关性

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Correlation between Ambulatory Arterial Stiffness Index and Carotid Atherosclerosis and Early Renal Damage in Patients with Essential Hypertension*

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ABSTRACT Objective: To investigate the correlation between ambulatory arterial stiffness index (AASI) and carotid atherosclerosis and early renal damage in patients with essential hypertension (EH). **Methods:** 147 patients with EH who were admitted to our hospital from June 2017 to May 2018 were selected as EH group. According to the difference of carotid artery intima-media thickness (IMT), the patients with $IMT \geq 1.0$ mm were recorded as carotid atherosclerosis group ($n=78$), and the patients with $IMT < 1.0$ mm were recorded as non-carotid atherosclerosis group ($n=69$). According to the difference of urine microalbumin (MAU) level, the patients with MAU level of 0~30 mg/24 h were recorded as MAU normal group ($n=86$), the patients with MAU level of 30~300 mg/24 h were recorded as MAU elevation group ($n=61$). Another 60 healthy volunteers in our hospital during the same period were selected as control group. The clinical data of EH group and control group were compared. The AASI and carotid artery elasticity function parameters in carotid atherosclerosis group and non-carotid atherosclerosis group were compared in EH patients. The AASI and renal function indexes of MAU normal group and MAU elevation group were compared. Pearson correlation analysis was used to analyze the correlation between AASI and carotid atherosclerosis and early renal damage in EH patients. **Results:** The smoking number, diabetes number, systolic blood pressure, diastolic blood pressure, IMT, AASI and MAU in the EH group were significantly higher than those in the the control group ($P < 0.05$). The AASI, pressure-strain elastic coefficient (Ep) and hardness index in the carotid atherosclerosis group were significantly higher than those in the

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non-carotid atherosclerosis group ($P<0.05$), vascular compliance (AC) was significantly lower than that in the non-carotid atherosclerosis group ($P<0.05$). The AASI in the MAU elevation group was significantly higher than that in the MAU normal group ($P<0.05$), PRO was significantly lower than that in the MAU normal group ($P<0.05$). But there were no significant differences in glomerular filtration rate (GFR) and creatinine clearance rate (CCr) between the MAU elevation group and the MAU normal group ($P>0.05$). Pearson correlation analysis showed that, there were positive correlation between AASI and IMT, MAU, Ep and hardness index in the EH patients ($P<0.05$), there was a negative correlation with AC, PRO ($P<0.05$), there were no correlation with GFR and CCr ($P>0.05$). **Conclusion:** AASI in EH patients is closely related to carotid atherosclerosis and early renal damage, the clinic can be monitored through AASI, so it can understand the risk of cardiovascular events and the degree of target organ injury in patients as early as possible.

Key words: Essential hypertension; Ambulatory arterial stiffness index; Carotid atherosclerosis; Renal damage; Correlation

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前言

原发性高血压(Essential Hypertension, EH)是由多种病因引起的处于不断进展状态下的一类心血管综合征,与动脉粥样硬化密切相关^[1,2]。长期的血压升高会导致机体动脉血管壁增厚、硬化、僵硬增加、顺应性降低,从而引发严重的心脑以及肾脏等并发症,给人类生命健康带来严重威胁^[3,4]。颈动脉是动脉粥样硬化最常累及的部位之一,因此,检测评估原发性高血压患者的颈动脉粥样硬化程度,可有效提高患者预后。同时,高血压患者也往往由于肾功能不全而增加了心血管疾病的发生风险。动态动脉硬化指数(Ambulatory arterial stiffness index, AASI)是一种采用常规 24 h 动态血压检测数据反映动脉硬化程度的新指数^[5,6],近年来相关研究表明,AASI 与 EH 患者靶器官的损伤、心血管疾病发病率及死亡率密切相关^[7,8],但有关 AASI 与颈动脉粥样硬化及早期肾损害的关系尚未完全阐明,且相关报道并不多见。鉴于此,本研究通过探讨 EH 患者 AASI 与颈动脉粥样硬化及早期肾损害的相关性,以期为临床防治提供参考。

1 资料与方法

1.1 一般资料

选取 2017 年 6 月~2018 年 5 月期间我院收治的 147 例 EH 患者记为 EH 组。纳入标准:(1)所有患者均符合《中国高血压防治指南》中有关 EH 的相关诊断标准^[9];(2)患者舒张压 ≥ 90 mmHg 和(或)收缩压 ≥ 140 mmHg;(3)入院前未接受过相关降压治疗;(4)患者及其家属知情本研究,并签署同意书。排除标准:(1)已发生心脑血管疾病是高血压者;(2)继发性高血压者;(3)合并自身免疫性疾病者;(4)近期有手术史者;(5)心肝肾功能不全者;(6)伴有恶性肿瘤者。另选取同期于我院进行体检的健康志愿者 60 例记为对照组。本研究已获我院伦理学委员会批准进行。

1.2 方法

1.2.1 AASI 检测 收集所有研究对象年龄、性别、吸烟史、糖尿病史、身高、体重资料,采用德国 MOBIL-O-GRAPH 型动态血压检测仪监测 24 h 动态血压,袖带于左上臂绑住,白天每隔 20 min、夜间每隔 30 min 自动充气测压一次,记录数值。采集所有数据,以收缩压为自变量,以舒张压为应变量,计算回归斜率(β),其中 $AASI=1-\beta$ 。

1.2.2 颈动脉粥样硬化 采用 GE 公司 VividE9 彩色多普勒超声诊断仪测定研究对象的颈动脉内中膜厚度(Intima-media thickness, IMT),探头频率为 9.0 MHz,IMT 以及血管内径在颈总动脉距分叉处近心 1 cm 及远心 1 cm 处测定,取左右两侧共 6 点平均值作为颈动脉 IMT,IMT ≥ 1.0 mm 表明存在颈动脉内膜增厚。将 IMT ≥ 1.0 mm 的患者记为颈动脉硬化组($n=78$),IMT < 1.0 mm 的患者记为无颈动脉硬化组($n=69$)。在二维模式下,当颈动脉中段纵断面处于最大断面时开启 ET 模式,待连续获得 5 个以上稳定波形曲线时保留图像,采用 e-DMS 系统自动计算硬度指数、血管压力应变弹性系数(Ep)、血管顺应性(AC)等颈动脉弹性功能参数。所有研究对象的检测均由同一名医生完成。

1.2.3 尿微量白蛋白检测 于清晨 7:00~次日 7:00 收集所有研究对象尿液,放入预先加有 10 mL 甲苯的容器内,混合均匀,测量 1 d 尿液总量,随后取 2 mL 送检。采用罗氏 Modular 全自动生化分析仪检测尿微量白蛋白(Microalbuminuria, MAU)水平,采用 99m TC-DTPA 肾动态显像测定肾小球滤过率(Glomerular filtration rate, GFR),采用碱性苦味酸动力学法检测血清肌酐,并计算肌酐清除率(Creatinine clearance rate, CCr),采用终点法检测尿蛋白定性(Protein, PRO),试剂盒由上海第二医科大学制药厂提供。根据患者 MAU 水平的不同,将 MAU 水平为 0~30 mg/24 h 的患者记为 MAU 正常组($n=86$),MAU 水平为 30~300 mg/24 h 的患者记为 MAU 升高组($n=61$)。

1.3 统计学处理

采用 SPSS23.0 统计学软件对研究数据进行处理。计量资料以($\bar{x} \pm s$)表示,行 t 检验,计数资料以[n(%)]表示,行 χ^2 检验,采用 Pearson 相关性分析 AASI 与颈动脉粥样硬化及早期肾损害相关性。 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 EH 组与对照组临床资料比较

两组研究对象男女比例、年龄、体重指数比较差异无统计学意义($P>0.05$),EH 组吸烟人数、糖尿病人数、收缩压、舒张压、IMT、AASI、MAU 显著高于对照组($P<0.05$),如表 1。

2.2 EH 患者中颈动脉硬化组、无颈动脉硬化组 AASI 以及颈动脉弹性功能参数比较

颈动脉硬化组 AASI、Ep、硬度指数均显著高于无颈动脉硬化组($P<0.05$),AC 明显低于无颈动脉硬化组($P<0.05$),如表 2。

表 1 EH 组与对照组临床资料比较

Table 1 Comparison of clinical data between the EH group and the control group

Groups	Male / female	Age (year)	Body mass index(kg/m ²)	Smoking	Diabetes	Systolic pressure (mmHg)	Diastolic blood pressure (mmHg)	IMT(mm)	AASI	MAU (mg/24 h)
Control group (n=60)	28/32	52.38±4.16	22.46±0.75	8	11	125.89±11.16	85.72±4.28	0.83±0.41	0.41±0.11	21.51±2.36
EH group (n=147)	76/71	51.93±5.85	22.58±0.91	42	53	167.46±15.34	103.93±8.68	1.15±0.32	0.57±0.15	126.09±33.84
x ² /t	0.432	0.542	0.903	5.400	6.265	19.025	15.484	5.997	7.478	23.880
P	0.511	0.588	0.367	0.020	0.012	0.000	0.000	0.000	0.000	0.000

表 2 EH 患者中颈动脉硬化、无颈动脉硬化者 AASI 以及颈动脉弹性功能参数比较($\bar{x} \pm s$)

Table 2 Comparison of AASI and carotid artery elasticity function parameters between carotid atherosclerosis and non-carotid atherosclerosis in EH patients($\bar{x} \pm s$)

Groups	AASI	Ep(Kpa)	AC(mm ² /Kpa)	Hardness index
Carotid atherosclerosis group(n=78)	0.62±0.13	176.53±34.26	0.68±0.13	15.28±2.30
Non-carotid atherosclerosis group(n=69)	0.51±0.18	76.80±18.46	1.49±0.52	7.11±1.08
t	4.300	21.564	13.301	26.984
P	0.000	0.000	0.000	0.000

2.3 EH 患者中 MAU 正常、MAU 升高者 AASI 及肾功能指标比较

显著低于 MAU 正常组(P<0.05), MAU 升高组与 MAU 正常组 GFR、CCr 比较差异无统计学意义(P>0.05), 如表 3。

MAU 升高组 AASI 显著高于 MAU 正常组(P<0.05), PRO

表 3 EH 患者中 MAU 正常、MAU 升高者 AASI 及肾功能指标比较($\bar{x} \pm s$)

Table 3 Comparison of AASI and renal function in patients with MAU normal and MAU elevation in EH patients($\bar{x} \pm s$)

Groups	AASI	GFR(ml/min)	CCr(μ mol/L)	PRO(mg/L)
MAU normal group(n=86)	0.52±0.10	85.56±8.72	70.63±7.22	110.21±15.12
MAU elevation group(n=61)	0.63±0.12	84.98±7.09	69.52±8.59	70.69±9.25
t	4.304	0.429	0.848	18.138
P	0.000	0.699	0.398	0.000

2.4 AASI 与颈动脉粥样硬化及早期肾损害的相关性分析

经 Pearson 相关性分析显示, EH 患者中 AASI 与 IMT、MAU、Ep、硬度指数均呈正相关性($r=0.435, 0.469, 0.461, P=0.000, 0.000, 0.000, 0.000$); 与 PRO、AC 呈负相关($r=-0.505, -0.512, P=0.000, 0.000$); 与 GFR、CCr 无相关性($r=-0.126, -0.206, P=0.165, 0.139$)。

3 讨论

EH 患者由于长期的血压升高, 血管壁受到压迫, 从而导致血管结构变化进程加速, 进一步使患者发展为动脉粥样硬化, 而动脉粥样硬化与血压相互作用最终将引发各种心脑血管疾病^[10,11]。颈动脉作为连接心脑两个重要器官的血管, 在动脉粥样硬化的发生、发展过程最早被累及, 颈动脉粥样硬化的形成是一种长期发展的过程, EH 是其发病的主要危险因素之一^[12,13]。据相关报道统计, 高血压患者导致的颈动脉粥样硬化发病率是血压正常者的 3~4 倍^[14]。目前临床颈动脉粥样硬化的评估指标

主要包括增强指数、脉压以及脉搏波传导速度, 虽然各指标灵敏度较好, 但上述指标检查存在操作难度大、费用高等缺陷, 在一定程度上限制了其在临床的广泛应用^[15,16]。近年来, AASI 的监测已逐渐受到临床医师的关注, 蔡文花等学者研究表明, 针对 EH 患者颈动脉粥样硬化进行分层, 可以及早预测心血管事件的发生情况^[17]。另杜国峰等学者研究也认为, AASI 可作为 EH 患者早期靶器官损伤的预测指标之一^[18]。肾损害是 EH 患者靶器官损伤的表现之一, 当血肌酐水平迅速上升时, 提示患者肾功能往往已经受损较为严重^[19]。相关研究表明, EH 患者颈动脉粥样硬化早期即可出现 MAU 升高^[20], 因此, 为了降低靶器官的损伤程度, 对 EH 患者进行 MAU 的监测也显得很有必要。

本次研究结果显示, EH 组吸烟人数、糖尿病人数、血压、IMT、AASI、MAU 显著高于对照组, 提示 EH 患者与高血压、吸烟、糖尿病、颈动脉粥样硬化及早期肾损害情况等多种危险因素息息相关。而颈动脉硬化组 AASI、Ep、硬度指数均显著高于无颈动脉硬化组, AC 明显低于无颈动脉硬化组, 说明颈动脉硬

化患者颈动脉弹性明显降低。Ep 可反映动脉血管弹性,血管发生硬化时,其值将升高,而硬度指数则用于反映颈动脉血管的硬化程度,其值越高则血管硬化越严重,AC 则反映血管顺应性,其值越低则血管硬化越严重,而 AASI 作为新的观测动脉硬化指标,可较好的反映压力容量曲线整体状态,是对血管壁和僵硬度的整体效果评估,因而其可以反映动脉管壁的内在情况^[20],既往研究证实,当动脉硬化程度越严重时,AASI 值则越趋近于 1^[22]。MAU 升高组 AASI 显著高于 MAU 正常组,PRO 显著低于 MAU 正常组,MAU 升高组与 MAU 正常组 GFR、CCr 比较差异无统计学意义。提示肾功能指标并不能较好的预测 EH 患者早期肾损害情况,而 AASI 具有较好的预测效果。EH 患者早期表现为全身细动脉硬化,而随着病情的进展,患者全身细动脉硬化,血管僵硬缺乏弹性,管腔狭窄,从而致使输送至组织的血流变慢,进而将引发心、脑、肾等靶器官供血受损,而此类受损将由最初的组织结构变化演变为功能代偿期,最后可能发展至功能失代偿期^[23,24]。Chin HJ 等^[25]通过对未经治疗的 EH 患者进行研究,发现 AASI 与尿蛋白呈正相关,与本研究结果一致,提示 AASI 可预测早期肾损害的发生情况。另外,经 Pearson 相关性分析显示,EH 患者中 AASI 与 IMT、MAU、Ep、硬度指数均呈正相关性,与 PRO、AC 呈负相关,而与 GFR、CCr 无相关性,表明 AASI 与患者颈动脉硬化和早期肾损害均存在相关性。由于 EH 患者血压长期升高,导致其血管内皮功能受损、血管平滑肌细胞增生以及血小板聚集能力减弱,从而使得患者内膜粗糙增厚,进而导致 IMT 增厚、血管弹性降低、硬化以及顺应性变差。而 EH 患者早期肾损害的主要病理变化表现为动脉硬化,肾动脉硬化是各种肾脏疾病以及全身血管病变进展到一定程度的共同病理变化,患者最终将演变为肾功能不全后反过来作用于 EH 患者,进一步加重病情,因此,临床可通过监测 AASI,有助于早期干预,以提高 EH 患者预后。

综上所述,EH 患者 AASI 与颈动脉粥样硬化及早期肾损害情况存在一定的相关性,临床可对 EH 患者进行 AASI 评估,有助于了解患者颈动脉粥样硬化程度,以预防心血管事件的发生,同时,对动脉硬化引起的靶器官损伤也具有一定的预测价值。

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