·临床研究·

老年高血压患者长时血压变异性及降压治疗对动脉僵硬度的影响

薛玉婷,任洁*

(山西医科大学第三医院·山西白求恩医院·山西医学科学院·同济山西医院心血管内科,太原 030032)

【摘 要】 **目的** 探讨长时血压变异性(BPV)和降压治疗对动脉僵硬度的影响。**方法** 选取2017年1月至6月于山西白求恩医院进行降压治疗及管理的原发性老年高血压患者411例,用臂踝脉搏波传导速度(baPWV)和踝臂指数(ABI)作为评估动脉僵硬度的指标。采用线性回归分析血压指数及BPV与baPWV、ABI的相关性,BPV用收缩压标准差(SBP_SD)表示。采用SPSS 26.0统计软件进行数据分析。采用t检验分析降压治疗的效果以及降压治疗对动脉僵硬度的影响。**结果** 通过3年降压治疗,老年高血压患者平均SBP、DBP、PP、MAP均较治疗前出现明显下降,FPG、TC、TG也较前明显下降,HDL-C较前明显升高,差异均有统计学意义[(131.78±7.36)和(142.92±17.14)mmHg(1 mmHg=0.133 kPa),(80.22±6.31)和(81.49±10.01)mmHg,(51.57±7.81)和(61.43±14.06)mmHg,(97.41±5.57)和(101.97±10.98)mmHg,(5.30±1.67)和(5.81±1.69)mmol/L,(3.85±0.95)和(4.42±0.90)mmol/L,(1.27±0.68)和(1.79±1.13)mmol/L,(1.35±0.31)和(1.21±0.31)mmol/L;均$P<0.05$];而治疗前后LDL-C的差异无统计学意义。调整混杂因素后线性回归结果显示,在老年高血压患者中SBP、PP、MAP、SBP_SD均与baPWV呈正相关($\beta=10.390, 5.500, 14.940, 11.110$;均$P<0.05$),与ABI呈负相关($\beta=-0.002, -0.001, -0.002, -0.003$;均$P<0.05$);而DBP仅与baPWV呈正相关($\beta=8.690$,$P<0.05$),而与ABI无相关性。降压治疗后,baPWV由(1782.70±308.87)cm/s降至(1732.43±261.73)cm/s、ABI由(1.12±0.10)升至(1.14±0.08),差异均有统计学意义(均$P<0.05$);其中baPWV在性别和年龄分层分析中均表现出下降趋势,与降压治疗前相比,差异均有统计学意义(均$P<0.05$);而ABI在女性患者及60~70岁患者中,与降压治疗前相比,差异均有统计学意义(均$P<0.05$)。降压前后SBP差值、DBP差值与baPWV差值均呈正相关($\beta=3.000, 3.290$;$P<0.05$),而与ABI差值无相关性。**结论** SBP_SD是动脉僵硬度的影响因素,对老年高血压患者进行降压治疗及综合管理,可以显著改善患者的baPWV值,而降压治疗对ABI的影响尚需进一步的研究去明确。

【关键词】 高血压;动脉僵硬度;降压治疗;长时血压变异性

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Effect of long-term blood pressure variability and anti-hypertensive treatment on arterial stiffness in elderly hypertensive patients

XUE Yu-Ting, REN Jie*

(Department of Cardiology, Third Hospital of Shanxi Medical University, Shanxi Bethune Hospital, Shanxi Academy of Medical Sciences, Tongji Shanxi Hospital, Taiyuan 030032, China)

【**Abstract**】 **Objective** To explore the effect of long-term blood pressure variability and anti-hypertensive treatment on arterial stiffness. **Methods** A total of 411 elderly patients with essential hypertension who were treated and managed in our hospital from January to June 2017 were enrolled in this study. Brachial-ankle pulse wave velocity (baPWV) and ankle-brachial index (ABI) were used as indicators to evaluate arterial stiffness. Linear regression analysis was employed to analyze the correlations of blood pressure index and long-term blood pressure variability (BPV) with baPWV and ABI. BPV was expressed as systolic blood pressure standard deviation (SBP_SD). SPSS statistics 26.0 was applied for data analysis. The efficacy of anti-hypertensive therapy and the effect of antihypertensive therapy on arterial stiffness were analyzed by student's t test. **Results** In those elderly patients with hypertension, 3 years' anti-hypertensive treatment resulted in significantly decreased average systolic blood pressure [SBP, (131.78±7.36) *vs* (142.92±17.14) mmHg(1 mmHg=0.133 kPa)], diastolic blood pressure [DBP, (80.22±6.31) *vs* (81.49±10.01) mmHg], pulse pressure [PP, (51.57±7.81) *vs* (61.43±14.06) mmHg] and mean artery pressure [MAP, (97.41±5.57) *vs* (101.97±10.98) mmHg], obviously reduced fasting plasma glucose [FPG, (5.30±1.67) *vs* (5.81±1.69) mmol/L], total cholesterol [(3.85±0.95) *vs* (4.42±0.90) mmol/L] and triglyceride [(1.27±0.68) *vs* (1.79±1.13) mmol/L], but remarkably elevated high-density lipoprotein cholesterol [(1.35±0.31) *vs* (1.21±0.31) mmol/L] when compared the corresponding values before treatment (all $P<0.05$). No such statistical change was seen in low-density lipoprotein cholesterol level before and after treatment. After adjustment for confounding

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通信作者: 任洁, E-mail: renjie1011@163.com

factors, SBP, PP, MAP and SBP_SD were positively correlated with baPWV (β=10.390, 5.500, 14.940, 11.110, all P<0.05) and negatively with ABI (β=-0.002, -0.001, -0.002, -0.003, all P<0.05) in the patients. DBP was only positively correlated with baPWV (β=8.690, P<0.05), but had no correlation with ABI. After antihypertensive treatment, baPWV was decreased from (1 782.70±308.87) cm/s to (1 732.43±261.73) cm/s, and ABI was increased from (1.12±0.10) to (1.14±0.08), with statistically differences (both P<0.05). Among them, baPWV showed a downward trend in gender and age stratifications, and significant difference was seen compared with that before antihypertensive treatment (P<0.05). ABI in the female patients and those aged 60-70 years was significantly different from that before anti-hypertensive treatment (P<0.05). The SBP difference and DBP difference before and after treatment were positively correlated with the difference of baPWV (β=3.000, 3.290, P<0.05), but not with the difference of ABI. **Conclusion** SBP_SD is an influencing factor of arterial stiffness. The antihypertensive treatment and comprehensive management of elderly hypertensive patients can significantly improve their baPWV value, but the effect on ABI needs further research to clarify.

【Key words】 hypertension; arterial stiffness; anti-hypertensive treatment; long-term blood pressure variability

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Corresponding author: REN Jie, E-mail: renjie1011@163.com

在全球范围内,高血压是导致心血管疾病和过早死亡的主要原因,且其患病率和血压水平随年龄的增长而增加[1]。众所周知,高血压与动脉僵硬之间存在相关性[2],且衰老也会导致动脉血管结构和功能的改变[3],使动脉顺应性下降,弹性层破裂[4],从而导致动脉僵硬度增加。有研究显示,收缩压(systolic blood pressure, SBP)、舒张压(diastolic blood pressure, DBP)、脉压(pulse pressure, PP)和平均动脉压(mean artery pressure, MAP)与臂踝脉搏波传导速度(brachial-ankle pulse wave velocity, baPWV)及踝臂指数(ankle-branchial index, ABI)均有相关性,并且随着SBP的上升,baPWV逐渐升高,ABI逐渐降低[5,6]。老年高血压患者由于受年龄及血压水平的双重影响,动脉血管功能更易受影响[7]。因此,明确降压治疗是否能改善动脉僵硬度对老年高血压患者的远期预后至关重要。baPWV及ABI因具有简便易行、有效性高及重复性高等优点,在临床上被广泛应用于评价动脉僵硬度[7]。本研究通过对老年高血压患者进行3年的降压治疗及管理,分析长时血压变异性(long-term blood pressure variability, BPV)对动脉僵硬度的影响以及明确降压治疗是否可以改善动脉僵硬度。

1 对象与方法

1.1 研究对象

选取2017年1月至6月于山西白求恩医院高血压门诊就诊的60~80岁的原发性高血压患者411例,签署知情同意书后,对所有患者行降压治疗,治疗期间对患者的管理采取网络管理与门诊管理相结合的方式。每3个月门诊随访1次,对患者的血压控制水平及用药情况进行调整。

纳入标准:(1)原发性高血压患者,包括首次诊断的高血压患者,要求3次门诊血压平均SBP均≥140 mmHg(1 mmHg=0.133 kPa)或正在接受降压治疗的高血压患者;(2)自愿参加,签署知情同意书。

排除标准:(1)SBP≥190 mmHg,或DBP<60 mmHg;(2)有卒中病史(除外腔隙性梗死和短暂性脑缺血发作);(3)已经确诊是继发性高血压;(4)近6个月内因急性心肌梗死或不稳定性心绞痛住院治疗;(5)近12个月内曾实施血运重建手术或在未来6个月内计划实施血运重建手术;(6)确诊过心脏方面疾病,如心律失常、肥厚型心脏病、严重瓣膜疾病等;(7)筛查时伴有心功能Ⅲ、Ⅳ级的心力衰竭或近6个月内因慢性心力衰竭加重而住院治疗;(8)糖尿病控制不佳,空腹血糖(fasting plasma glucose, FPG)≥200 mg/dl或糖化血红蛋白>8%;(9)严重肝肾疾病或有恶性肿瘤病史。

1.2 方法

1.2.1 基线数据 采用问卷调查收集患者的姓名、性别、年龄、个人史、家族史及生活习惯(如吸烟、饮酒状况)等,行一般检查如身高、体质量、腰围及血压等。体质量指数(body mass index, BMI)=体质量(kg)/身高(m)^2。

1.2.2 血压测量 按照标准血压测量方法,统一使用欧姆龙(OMRON)上臂式电子血压计为患者测量门诊血压。测量前30 min内禁止吸烟、饮茶、喝咖啡,静坐休息5~10 min。连续测量2次,间隔1~2 min,取2次读数的平均值。若2次读数相差5 mmHg,则测量第3次,取3次读数的平均值。

1.2.3 长时血压变异性 一般指数日、数周、数月、季节和数年间的血压波动程度。本研究的BPV是指3年随访期间的血压波动程度,患者在入组前3个月每个月随访1次,以后每3个月门诊随访1次。

本研究选取SBP标准差(standard deviation, SD)表示BPV,SBP_SD=

$$\sqrt{(SBP_{1年}-SBP_{均数})^2+(SBP_{2年}-SBP_{均数})^2(SBP_{3年}-SBP_{均数})^2/3}$$

其中$SBP_{1年}$为患者入组第1年度平均SBP,$SBP_{2年}$为患者入组第2年度平均SBP,$SBP_{3年}$为患者入组第3年度平均SBP,$SBP_{均数}$为3次SBP的均值。

1.2.4 生化指标的测量 采集患者空腹静脉血5 ml,采用日立7170型全自动生化仪检测FPG、胆

固醇(total cholesterol, TC)、甘油三酯(triglyceride, TG)、低密度脂蛋白胆固醇(low-density lipoprotein cholesterol, LDL-C)、高密度脂蛋白胆固醇(high-density lipoprotein cholesterol, HDL-C)等指标。

1.2.5 baPWV、ABI 的测定 检测时,患者取平卧位,上臂袖带气囊对准肱动脉,下肢袖带气囊位于下肢内侧。本研究选取读数较大的一侧 baPWV、ABI 进行分析,本研究将 baPWV≥1400 cm/s 作为动脉硬化的诊断标准,ABI≤0.9 作为下肢血管堵塞的诊断标准。

1.3 统计学方法

采用 SPSS 26.0 统计软件进行数据分析。计量资料用均数±标准差($\bar{x}\pm s$)表示,采用 t 检验。采用线性回归分析血压指数及 SBP_SD 与 baPWV 和 ABI 之间的关系。$P<0.05$ 为差异有统计学意义。

2 结 果

2.1 老年高血压患者的基线特征

最终纳入患者 362 例。其中男性 160 例,女性 202 例;平均年龄(65.04±4.40)岁;平均 BMI(26.03±3.20)kg/m^2;平均腰围(89.95±9.48)cm;高血压病史(13.85±10.49)年;平均 baPWV(1782.70±308.87)cm/s;平均 ABI(1.12±0.10)。

2.2 老年高血压患者降压治疗前后比较

与降压治疗前比较,老年高血压患者在降压治疗后,平均 SBP、DBP、PP、MAP 均出现明显下降,FPG、TC、TG 也较术前明显下降,HDL-C 也较术前升高,差异均有统计学意义(均 $P<0.05$);而治疗前后 LDL-C 的差异无统计学意义(表 1)。

2.3 血压指数及 SBP_SD 与 baPWV、ABI 的相关性

对 3 年平均 SBP、DBP、PP、MAP 及 SBP_SD 分别与治疗后 baPWV 及 ABI 做相关性分析,将上述血压指数作为自变量纳入线性回归分析。调整混杂因素前,SBP、PP、MAP、SBP_SD 均与 baPWV 呈正相关,与 ABI 呈负相关(均 $P<0.05$),DBP 与 baPWV、ABI 均无相关性($P>0.05$);调整混杂因素后,SBP、PP、MAP、SBP_SD 与 baPWV 呈正相关,与 ABI 呈负相关(均 $P<0.05$),而 DBP 与 baPWV 呈正相关($P<0.05$),与 ABI 无相关性(表 2)。

表 1 老年高血压患者降压治疗前后比较

Table 1 Comparison of antihypertensive therapy in elderly patients with hypertension ($n=362$, $\bar{x}\pm s$)

Variable	Average SBP (mmHg)	Average DBP (mmHg)	Average PP (mmHg)	Average MAP (mmHg)	FPG (mmol/L)	TC (mmol/L)	TG (mmol/L)	LDL-C (mmol/L)	HDL-C (mmol/L)
Baseline level	142.92±17.14	81.49±10.01	61.43±14.06	101.97±10.98	5.81±1.69	4.42±0.90	1.79±1.13	2.60±0.74	1.21±0.31
Level after antihypertensive treatment	131.78±7.36	80.22±6.31	51.57±7.81	97.41±5.57	5.30±1.67	3.85±0.95	1.27±0.68	2.51±0.81	1.35±0.31
t	12.119	2.697	15.169	7.859	4.505	8.789	7.513	1.477	−8.081
P value	0.000	0.007	0.000	0.000	0.000	0.000	0.000	0.141	0.000

SBP: systolic blood pressure; DBP: diastolic blood pressure; PP: pulse pressure; MAP: mean arterial pressure; FPG: fasting plasma glucose; TC: total cholesterol; TG: triglyceride; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol.

表 2 血压指数与 baPWV、ABI 的线性回归分析

Table 2 Linear regression analysis of blood pressure index with baPWV and ABI

Independent variable	baPWV after treatment			ABI after treatment		
	β	95%*CI*	P value	β	95%*CI*	P value
Unadjusted						
Three years average SBP	9.870	6.470−3.270	0.000	−0.002	−0.003−0.001	0.001
Three years average DBP	3.600	−1.050−8.260	0.129	−0.001	−0.002−0.001	0.226
Three years average PP	6.330	3.190−9.460	0.000	−0.001	−0.002−0.000	0.039
Three years average MAP	10.500	5.290−15.720	0.000	−0.002	−0.004−0.000	0.011
SBP_SD	12.760	5.670−19.850	0.000	−0.002	−0.005−0.000	0.028
Adjusted						
Three years average SBP	10.390	6.880−13.890	0.000	−0.002	−0.003−0.001	0.001
Three years average DBP	8.690	3.610−13.770	0.001	−0.001	−0.003−0.000	0.175
Three years average PP	5.500	2.03−8.96	0.002	−0.001	−0.002−0.000	0.023
Three years average MAP	14.940	9.55−20.33	0.000	−0.002	−0.004−0.001	0.007
SBP_SD	11.110	3.92−18.30	0.003	−0.003	−0.005−0.000	0.022

Unadjusted baPWV, ABI as dependent variables; SBP, DBP, PP, MAP, SBP_SD as independent variables. Adjusted for gender, age, BMI, FBG, TC, TG, HDL-C. baPWV: brachial-ankle pulse wave velocity; ABI: ankle-brachial index; SBP: systolic blood pressure; DBP: diastolic pressure; PP: pulse pressure; MAP: mean arterial pressure; SBP_SD: standard deviation of systolic pressure; BMI: body mass index; FBG: fasting blood glucose; TC: total cholesterol; TG: triglyceride; HDL-C: high-density lipoprotein cholesterol.

2.4 老年高血压患者降压治疗前后 baPWV 和 ABI 的比较

与降压治疗前相比,老年高血压患者治疗后的平均 baPWV 有所下降,平均 ABI 有所上升,差异均有统计学意义(均 $P<0.05$)。无论从性别还是年龄分层,baPWV 都呈现显著下降,差异均有统计学意义(均 $P<0.05$);而 ABI 在女性、60~70 岁患者中呈现上升趋势(均 $P<0.05$),而在男性、71~80 岁患者中差异均无统计学意义(表 3)。

表 3 老年高血压患者降压治疗前后 baPWV 和 ABI 的比较

Table 3 Comparison of baPWV and ABI before and after antihypertensive treatment in elderly hypertensive patients

($n=362$, $\bar{x}\pm s$)

Variable	Baseline level	Level after antihypertensive treatment	t	P value
baPWV (cm/s)				
Overall	1 782.70±308.87	1 732.43±261.73	3.584	0.000
Male	1 752.07±327.35	1 706.05±275.04	2.160	0.032
Female	1 806.96±291.96	1 753.32±249.39	2.873	0.000
60-70 years	1 758.95±293.61	1 728.25±259.86	2.095	0.037
71-80 years	1 938.06±360.91	1 759.75±274.89	4.410	0.000
ABI				
Overall	1.12±0.10	1.14±0.08	-3.052	0.002
Male	1.13±0.11	1.15±0.08	-1.691	0.093
Female	1.12±0.09	1.13±0.07	-2.620	0.009
60-70 years	1.12±0.10	1.14±0.08	-2.643	0.009
71-80 years	1.12±0.10	1.14±0.09	-1.620	0.112

baPWV: brachial-ankle pulse wave velocity; ABI: ankle-branchial index.

2.5 老年高血压患者降压治疗前后血压差值与 baPWV、ABI 差值的线性回归分析

对降压治疗前后 SBP 差值、DBP 差值与 baPWV 差值、ABI 差值做相关性分析,将上述血压差值作为自变量纳入线性回归分析。调整混杂因素前,SBP 差值与 baPWV 差值呈正相关($P<0.05$),与 ABI 差值无相关性,DBP 差值与 baPWV 差值和 ABI 差值均无相关性(均 $P>0.05$);调整混杂因素后,SBP 差值、DBP 差值与 baPWV 差值均呈正相关(均 $P<0.05$),而与 ABI 差值均无相关性(均 $P>0.05$;表 4)。

3 讨 论

动脉僵硬度是动脉壁功能和结构变化的最早检测指标之一,并被认为是心血管和全因死亡的直接和独立预测因子。若能有效控制动脉僵硬度的发生发展,有可能会降低心血管疾病和全因死亡的发生率。众所周知,动脉僵硬度与高血压之间关系密切。高血压可以促进动脉僵硬度的发生,但降压治疗是否可以逆转动脉僵硬度目前尚未明确。

大量研究已经证实动脉僵硬度的影响因素多种多样,其中包括年龄、性别、BMI、血糖及血脂等。Chen 等[10]的研究表明,baPWV 会随年龄增长而增加,并且在 65 岁以后增加速度会加快。高 BMI 是血管老化的一个保护因素,而血管老化会进一步导致动脉硬化,因此,高 BMI 也对动脉僵硬度有一定的保护作用[11]。血糖可能通过炎症和氧化应激反应促进动脉僵硬度的增加[12]。CSPPT 研究显示,随着 TC、TG 的升高和 HDL-C 的下降,baPWV 随之升高,而 LDL-C 与动脉僵硬度之间没有相关性[13]。衰老、肥胖等因素又会进一步导致动脉僵硬度的发展产生性别差异,并且雌激素对动脉僵硬度有调节作用,女性在绝经以后动脉僵硬度会比男性增加的更快[14]。鉴于上述因素对动脉僵硬度的影响,本研究在分析降压治疗对动脉僵硬度的影响时,对上述因素均作了调整,以使结果更加客观。

本研究发现,随着血压水平的增加,动脉僵硬度和血管壁厚度逐渐升高,与一些国内外研究结果一致[5,15,16]。在对患者进行降压管理与治疗后,无论是从整体人群分析,还是按性别、年龄分层进行分析,baPWV 均有明显的改变,说明这种变化不受性别、年龄差异的影响。而对于 ABI 来说,从整体人群角度分析,降压治疗前后差异有统计学意义,但在分层分析时,仅在女性和 60~70 岁患者中差异有统计学意义,而男性和 70~80 岁患者中差异无统计学意义,我们需要进一步在不同的人群中明确这种结果是否有意义。为了明确 baPWV 和 ABI 的变化是否与降压治疗有关系,我们对治疗前后血压差值与

表 4 降压前后血压差值与 baPWV、ABI 差值的线性回归分析

Table 4 Linear regression analysis of blood pressure difference and baPWV, ABI difference before and after hypotension

Independent variable	baPWV difference			ABI difference		
	β	95%CI	P value	β	95%CI	P value
Unadjusted						
SBP difference	0.022	-1.470-1.510	0.029	4.340	0.000-0.000	0.189
DBP difference	-1.900	-4.620-0.810	0.169	-3.160	-0.001-0.001	0.994
Adjusted						
SBP difference	3.000	1.510-4.460	0.000	0.000	-0.001-0.001	0.714
DBP difference	3.290	0.570-6.000	0.018	-0.001	-0.002-0.000	0.154

Unadjusted baPWV and ABI difference as dependent variables, SBP difference and DBP difference as independent variables; adjusted for gender, age, BMI, FBG, TC, TG, HDL-C. baPWV: brachial-ankle pulse wave velocity difference; ABI: ankle-brachial index difference; SBP: systolic blood pressure; DBP: diastolic pressure; BMI: body mass index; FBG: fasting blood glucose; TC: total cholesterol; TG: triglyceride; HDL-C: high-density lipoprotein cholesterol.

baPWV、ABI 差值做了线性相关分析,结果显示老年高血压患者的 baPWV 的改变跟血压的下降有关,但 ABI 的改变与血压降低的相关性不明显。

近年来,许多研究表明血压变异性与心血管疾病风险相关,与短时血压变异性相比,BPV 可以更好地预测心脏、血管和肾脏损害的发生[17]。在本研究中,随着 BPV 的增加,动脉僵硬度与血管壁厚度逐渐升高,其原因可能是,BPV 的增加会诱导多种炎症因子表达,促进平滑肌细胞增殖,从而加速动脉硬化发生[18]。

综上,对老年高血压患者规范降压治疗,并且保持血压的平稳,可以有效改善动脉血管的弹性,降低心血管疾病的风险。本研究也存在一些局限性,首先,本研究没有采用颈-股动脉脉搏波传导速度进行检测,但已经证实 baPWV 与颈-股动脉脉搏波传导速度的相关性好,美国心脏协会也推荐 baPWV 作为评估动脉硬化的标准[19];其次,研究样本量较少,并且样本选择具有区域性。未来若有多中心、大样本的研究去支持这一结果,将对临床有更好的指导意义。

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