

· 临床研究 ·

老年高血压患者夜间血压模式短期可重复性的临床研究

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【摘要】目的 通过分析老年高血压患者动态血压监测 (ABPM) 夜间血压模式的可重复性, 评估其在临床应用中的实际意义。**方法** 对入住上海交通大学附属第六人民医院老年科70名老年高血压患者[男45例, 女25例, 年龄 (83.57 ± 5.37) 岁]于4周内进行两次24hABPM, 根据夜间血压下降率分为杓型 (D)、非杓型 (ND)、反杓型 (RD) 3种血压模式, 把夜间下降率分别作为连续性变量和分类变量来分析血压模式的短期可重复性, 并探究可重复的不同模式间的差异。**结果** 作为连续性变量, Bland-Altman图示夜间下降率可重复性较好; 作为分类变量, 第2次ABPM维持原来血压模式不变的受试者共占65.7% (46/70), 其中50.0% (14/28) 维持原来RD, 76.5% (13/17) 维持原来D, 76.0% (19/25) 维持原来ND, kappa值为0.482。第1次ABPM为RD、D和ND在第2次ABPM转变为其他模式的分别有20.0%, 5.7%和8.6%。可重复的RD (组1)、D (组2)、ND (组3) 与模式变换型 (组4) 两两之间比较的主要临床特点无明显差异。**结论** 老年高血压患者的夜间血压模式无论是作为分类变量还是连续变量, 可重复性都尚好, 且RD血压模式相比D或ND的变异性更高, 因此, 临床上我们不可以仅凭一次ABPM就评定患者的血压模式。本研究尚未发现可能影响血压模式重复性的因素。

【关键词】 老年人; 夜间血压模式; 可重复性

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Short-term reproducibility of nocturnal blood pressure pattern in elderly essential hypertensive patients

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【Abstract】 Objective To analyze the reproducibility of nocturnal blood pressure pattern in the elderly hypertensive patients by ambulatory blood pressure monitoring (ABPM) and evaluate its significance in clinical practice. **Methods** A total of 70 elderly essential hypertensive patients [45 males and 25 females, aged (83.57 ± 5.37) years] admitted in the Department of Geriatrics from the Sixth People's Hospital of Shanghai Jiaotong University were enrolled in this study. They underwent ABPM over two 24-hour periods within 4 weeks and other routine examinations. Their dipping patterns were classified as dippers (D), non-dippers (ND) and reverse-dipper (RD) according to their average systolic blood pressure at night compared to daytime. The short-term reproducibility was evaluated when above 3 different patterns used as continuous variables or categorical variables, and the differences among the reproducible and variable modes were analyzed. **Results** When the dipping patterns used as continuous variables, Bland-Altman's plot showed that the reproducibility was good. While as categorical variables, overall 65.7% of the total 70 subjects (46/70) showed consistent dipping pattern during the 2 periods of ABPM, including 50.0% (14/28) confirming the identical RD, 76.5% (13/17) the identical D, and 76.0% (19/25) the identical ND (kappa = 0.482). Subjects who had RD, D and ND on the first ABPM but changed to another pattern on the second time accounted for 20.0%, 5.7%, and 8.6%, respectively. No significant difference was found among the persistent RD (group 1), D (group 2), ND (group 3) and those with variable dippers (group 4) in main clinical characteristics. **Conclusion** The nocturnal blood pressure pattern is moderately reproducible in the elderly hypertensive patients, regardless of as continuous or categorical variable, but the reverse-dippers have higher variability when compared to dippers and non-dippers. Therefore, we should not confirm the dipping status based on single period of ABPM. This study has not found any factor that may affect the nocturnal dipping pattern.

【Key words】 elderly; nocturnal blood pressure; reproducibility

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24h动态血压检测(ambulatory blood pressure monitoring, ABPM)是通过24h持续监测血压水平,全面地了解患者血压水平和昼夜波动规律,在高血压的诊断、治疗和预后中,相比诊室血压和家庭自测血压显示出明显的优越性,尤其是ABPM夜间模式的判定有利于高血压患者靶器官损害和心脑血管事件风险的评估^[1-3]。虽然ABPM的可重复性较诊室血压高^[4],但关于夜间血压模式的可重复性程度如何,目前还存在争议。我们对老年原发性高血压患者于4周内进行两次ABPM,以评估血压昼夜节律的短期可重复性。

1 对象与方法

1.1 对象

选取入住上海交通大学附属第六人民医院老年科的年龄 ≥ 60 岁的老年原发性高血压患者,男45例,女25例,年龄(83.57 ± 5.37)岁。高血压诊断标准依据2010年《中国高血压防治指南》^[5]。纳入标准为入院前4周和住院期间未调整降压药、且血压控制比较稳定的高血压患者。排除标准:(1)继发性高血压;(2)高血压急症、严重心脏病;(3)新发心脑血管意外;(4)严重肝肾功能不全等各种慢性疾病的急性期或终末期;(5)严重心律失常(如房颤);(6)全天有效血压读数 $< 80\%$;(7)不能从事日常活动者。本试验经医院伦理委员会批准,所有研究对象均自愿参与并签署知情同意书。

1.2 研究方法

1.2.1 一般项目指标 性别、年龄、血糖、血脂、肌酐等。所有受试者隔夜空腹8h后测定一般血生化指标。

1.2.2 动态血压监测 本研究采用美国伟伦国际贸易公司的Welch Allyn ABPM 6100便携式动态血压监护仪,采用示波振荡法进行24h血压测量,即用袖带阻断动脉血流,检测起源于血管壁的搏动所引起的袖带内气体的振荡波,缚于非优势侧上臂,并尽量避免该侧肌肉活动和睡眠时被压迫,嘱受试者避免较大强度的活动以免影响读数的准确性。设定6:00~22:00为白天,22:00~6:00为夜间,并要求受试者早上6:00起床,晚上22:00睡觉。便携式动态血压监护仪自动充气,白天15min/次,夜间30min/次。4周内进行第2次24hABPM。

1.2.3 选取ABPM的常用参数 (1)24h平均收缩压(24-hour mean systolic blood pressure, 24hSBP),24h平均舒张压(24-hour mean diastolic blood pressure,

24hDBP);(2)日间平均收缩压(daytime mean systolic blood pressure, dSBP),日间平均舒张压(daytime mean diastolic blood pressure, dDBP);(3)夜间平均收缩压(nighttime mean systolic blood pressures, nSBP),夜间平均舒张压(nighttime mean diastolic blood pressure, nDBP);(4)24h平均脉压(24-hour mean pulse pressure, PP);(5)24h平均心率(24-hour mean heart rate, HR)。根据夜间血压下降率即 $(dSBP - nSBP) / dSBP$,将血压夜间模式分为3类:夜间血压下降率 $\geq 10\%$ 为杓型(dipper, D),即正常的生理昼夜节律;夜间血压下降率 $0\% \sim 10\%$ 表示昼夜节律减弱为非杓型(non-dipper, ND);夜间血压下降率 $< 0\%$ 为反杓型(reverse-dipper, RD)。

1.3 统计学处理

采用SPSS17.0软件进行统计分析。正态分布资料以 $(\bar{x} \pm s)$ 表示,偏态分布资料以中位数(四分位间距)表示。方差齐性的正态分布计量资料,两组间比较采用t检验,多组间比较采用单因素方差分析(one-way analysis of variance, one-way ANOVA),多样本均数的两两比较采用LSD法。重复性检验的计量资料用Bland-Altman,计数资料用卡方或一致性检验(kappa检验)。以 $P < 0.05$ 为差异具有统计学意义。

2 结果

2.1 受试者第1次和第2次ABPM常用参数的配对样本t检验

如表1所示,受试者第1次和第2次ABPM的平均血压值呈高度相关(相关系数 $r > 0.8$, $P > 0.05$)。

2.2 Bland-Altman法分析第1次和第2次ABPM的24hSBP和24hDBP的重复性

如图1和图2所示,中间水平实线代表两次ABPM 24h平均血压的差值,越接近0代表两次ABPM的一致程度越高。图1示 $10\% (7/70)$ 的点在95%一致性界限以外,在一致性界限以内,两次ABPM 24hSBP差值的绝对值最大为16mmHg(图中实心圆圈代表的点),而24hSBP的均值为125.95mmHg(表1)。图2示 $8.57\% (6/70)$ 的点在一致性界限以外,在一致性界限范围内,两次ABPM 24hDBP差值的绝对值最大为9mmHg($1\text{mmHg} = 0.133\text{kPa}$;图中实心圆圈代表的点),24hDBP的均值为64.05mmHg(表1)。这种相差幅度在临床上可以接受,因此可以认为24h平均血压具有较好的一致性。

表1 两次ABPM常用参数的配对t比较

Table 1 General parameters of blood pressure between the first and second ABPM ($n = 70$, mmHg, $\bar{x} \pm s$)

ABPM	24hSBP	24hDBP	PP	dSBP	dDBP	nSBP	nDBP
1st	125.9 ± 17.4	64.1 ± 10.0	62.0 ± 13.3	126.2 ± 16.5	64.6 ± 9.9	124.7 ± 23.0	62.0 ± 11.6
2nd	126.0 ± 17.3	64.0 ± 9.7	62.4 ± 14.6	127.6 ± 17.0	65.1 ± 10.0	123.4 ± 21.7	61.1 ± 10.8
1st-2nd	-0.029 ± 8.7	0.071 ± 4.8	-0.4543 ± 6.5	-1.429 ± 8.8	-0.543 ± 4.9	1.271 ± 12.7	0.9000 ± 6.0
<i>r</i>	0.873	0.883	0.895	0.863	0.879	0.84	0.859
<i>P</i>	0.978	0.901	0.562	0.179	0.357	0.405	0.213

ABPM: ambulatory blood pressure monitoring; 24hSBP: 24-hour mean systolic blood pressure; 24hDBP: 24-hour mean diastolic blood pressure; PP: 24-hour mean pulse pressure; dSBP: daytime mean systolic blood pressure; dDBP: daytime mean diastolic blood pressure; nSBP: nighttime mean systolic blood pressure; nDBP: nighttime mean diastolic blood pressure; 1st: the first ABPM; 2nd: the second ABPM; 1st-2nd: difference between the first and second ABPM; *r*: correlation coefficient between the first and second ABPM. 1mmHg = 0.133kPa

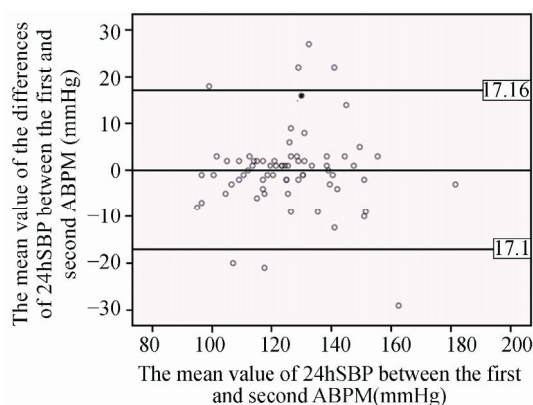


图1 两次ABPM 24hSBP的Bland-Altman图

Figure 1 Bland-Altman's plot of 24hSBP in the first and second ABPM

The horizontal line in the middle presents the mean value of the differences of 24hSBP ($\bar{d} = -0.029$) between the first and second ABPM; the two horizontal lines above and below present the upper and lower limits of 95% limits of agreement ($\bar{d} \pm 1.96S_{\bar{d}}$). ABPM: ambulatory blood pressure monitoring; 24hSBP: 24-hour mean systolic blood pressure

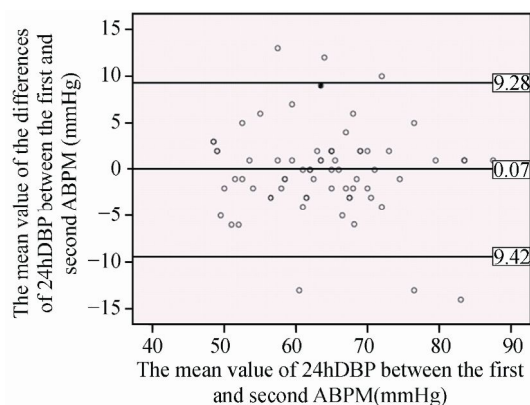


图2 两次ABPM 24hDBP的Bland-Altman图

Figure 2 Bland-Altman's plot of 24hDBP in the first and second ABPM

The horizontal line in the middle presents the mean value of the differences of 24hDBP ($\bar{d} = -0.071$) between the first and second ABPM; the two horizontal lines above and below present the upper and lower limits of 95% limits of agreement ($\bar{d} \pm 1.96S_{\bar{d}}$). ABPM: ambulatory blood pressure monitoring; 24hDBP: 24-hour mean diastolic blood pressure

2.3 作为分类变量分析夜间血压下降率的重复性

在70例受试者中, 第2次ABPM和第1次ABPM血压模式保持不变的共有65.7% (46/70), 其中50% (14/28) 维持原来的RD, 76% (13/17) 维持D, 76%

(19/25) 维持ND。由RD转变为D或ND共20% (14/70), D转变为RD或ND有5.7% (4/70), ND转变为D或RD共8.6% (6/70), $\kappa = 0.482$ ($P < 0.01$; 表2)。

表2 受试者第1次和第2次ABPM的夜间血压模式

Table 2 Nocturnal blood pressure pattern in the first and second ABPM (n)

Nocturnal pattern	2nd RD	2nd D	2nd ND
1st RD	14	1	13
1st D	1	13	3
1st ND	2	4	19

1st RD: subjects showing reverse-dipper in the first ABPM; 1st D: subjects showing dipper in the first ABPM; 1st ND: subjects showing non-dipper in the first ABPM; 2nd RD: subjects showing reverse-dipper in the second ABPM; 2nd D: subjects showing dipper in the second ABPM; 2nd ND: subjects showing non-dipper in the second ABPM

2.4 作为连续变量分析夜间血压下降率的重复性

若把nSBP/dSBP比值作为连续变量, 则两次ABPM nSBP/dSBP比值比的均数如越接近1, 表明两次ABPM测量的一致性程度越高。8.6% (6/70) 的点在95%一致性界限外; 一致性界限内, 比值最大为1.14, 最小为0.91 (如图3中实心圆圈代表的两个点)。

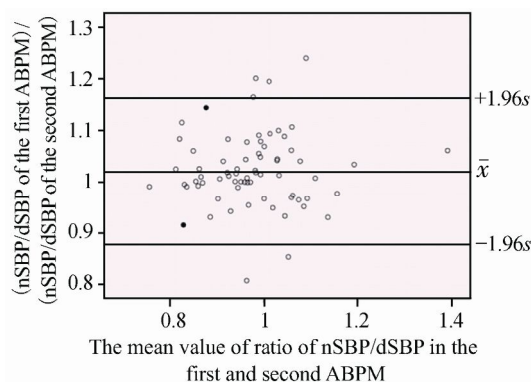


图3 据两次ABPM nSBP/dSBP比绘制的Bland-Altman图

Figure 3 Bland-Altman's plot of ratio of nSBP/dSBP in the first and second ABPM

The horizontal line in the middle presents the mean value of (nSBP/dSBP of the first ABPM)/(nSBP/dSBP of the second ABPM); the two horizontal lines above and below present the upper and lower limits of 95% limits of agreement ($\bar{x} \pm 1.96s$)

2.5 不同血压模式可重复组与变化组的临床特征的比较

对以下4组的连续性变量和分类变量分别做方差分析和卡方检验,除了变密度值蛋白胆固醇外,只有nSBP ($F = 11.059, P < 0.001$)和nDBP ($F = 8.247, P < 0.001$)存在显著性差异,且nSBP在组1、组2、组3两两之间都有显著差异 ($P < 0.01$),其他指标未见明显差异。

3 讨论

3.1 作为连续变量和分类变量分析夜间血压下降的短期可重复性

采用两种统计方法,第1次和第2次ABPM的24hSBP, 24hDBP, dSBP, dDBP nSBP和nDBP一致性较高(均 $r > 0.8$;表1),Bland-Altman图也显示24hSBP和24hDBP具有较好一致性(图1和图2)。当把夜间血压下降率作为分类变量时,两次ABPM血压模式保持一致的共有65.7%(表2),重复性尚可($\kappa = 0.482, P < 0.01$);作为连续变量时,nSBP/dSBP值第1次ABPM是第2次的0.91~1.14倍,

即对于大多数受试者,第1次相比第2次ABPM的nSBP/dSBP相差9%~14%(图3),从临床上考虑这种差异是可接受的,因此,无论是作为分类变量还是连续变量,夜间血压下降的短期重复性均较好。另外,Campbell等^[4]和McGowan等^[6]还发现其作为连续变量相比分类变量的长期重复性更高。本研究同时还发现, RD, D和ND型转变为其他模式的分别有20.0%, 5.7%和8.6%,可见RD相比其他模式的变异性更高。同样,Cuspidi等^[7]发现,在早期未经治疗的原发性高血压患病人群中,ND(含ND和RD)相比D的重复性也较差(72.2%ND→ND, 90.6%D→D);Hermida等^[8]在代谢综合征人群中也发现ND(含ND、RD)更易变化。有研究^[9]发现血压模式为RD的夜间高血压能预测心血管事件风险和死亡率,且相比D的死亡率更高。可见,多次进行ABPM以及早发现并纠正异常血压模式具有深远的临床意义。

3.2 可能影响血压昼夜节律可重复性的因素

先前有关血压昼夜模式可重复性的临床研究结

表3 4组不同血压模式的临床特点
Table 3 Clinical characteristics in repeated reverse-dippers, dippers, non-dippers and variable dippers ($\bar{x} \pm s$)

Item	Group 1(n = 14)	Group 2(n = 13)	Group 3(n = 19)	Group 4(n = 24)	F/χ^2	P
Age(years)	84.21 ± 5.47	82.85 ± 4.32	84 ± 5.82	83.38 ± 5.69	0.189	0.903
24hSBP(mmHg)	133.25 ± 15.82	121.12 ± 18.40	124.13 ± 18.90	125.77 ± 14.15	1.336	0.270
24hDBP(mmHg)	64.25 ± 7.89	61.27 ± 11.53	64.53 ± 10.97	65.06 ± 8.37	0.463	0.709
dSBP(mmHg)	131.25 ± 16.18	125.65 ± 18.02	125.34 ± 18.86	126.32 ± 13.24	0.421	0.738
dDBP(mmHg)	63.93 ± 8.07	63.62 ± 12.49	65.53 ± 10.93	65.54 ± 8.12	0.179	0.910
nSBP(mmHg)	144.21 ± 17.55 ^{***}	105.00 ± 15.09 ^{###▲▲}	121.16 ± 19.19 ^{**▲▲}	124.90 ± 18.30	11.059	0.000
nDBP(mmHg)	67.39 ± 8.67 ^{**}	50.65 ± 7.88 ^{###▲▲}	61.34 ± 10.65 ^{**}	64.17 ± 9.49	8.247	0.000
CR(μmol/L)	75.21 ± 17.02	78.54 ± 28.66	93.11 ± 25.20	83.46 ± 23.39	1.924	0.134
TC(mmol/L)	4.74 ± 1.11	4.16 ± 0.75	4.01 ± 0.84	4.23 ± 0.94	1.902	0.138
TG(mmol/L)	1.09 ± 0.58	1.23 ± 0.56	1.07 ± 0.42	1.43 ± 1.29	0.744	0.530
LDL-C(mmol/L)	2.79 ± 1.08	2.50 ± 0.75	2.27 ± 0.89	2.44 ± 0.87	1.115	0.349
HDL-C(mmol/L)	1.81 ± 0.89 ^{**###△△}	1.32 ± 0.51	1.26 ± 0.41	1.33 ± 0.45	2.980	0.038
Lpa(mmol/L)	11.90 ± 11.06	15.56 ± 17.07	16.95 ± 15.99	9.66 ± 6.90	1.353	0.265
FBG(mmol/L)	5.48 ± 0.86	5.59 ± 0.84	5.80 ± 1.40	6.32 ± 1.64	1.546	0.211
2hPBG(mmol/L)	8.14 ± 3.05	8.21 ± 1.87	8.67 ± 3.26	8.81 ± 3.16	0.914	0.439
HbA1c(%)	5.94 ± 1.12	6.35 ± 0.66	6.84 ± 1.23	6.83 ± 1.24	2.417	0.074
FT3(Pmol/L)	3.89 ± 0.45	4.00 ± 0.64	3.76 ± 0.49	4.19 ± 0.53	2.506	0.067
FT4(Pmol/L)	16.21 ± 3.88	15.35 ± 3.49	14.49 ± 1.85	16.35 ± 3.52	1.382	0.256
TSH(mIU/L)	2.71 ± 1.88	2.51 ± 1.86	2.59 ± 1.41	2.57 ± 1.60	0.035	0.991
male/female	7/7	10/3	8/11 ^{△△}	20/4	10.013	0.018
DM/non-DM	7/7	5/8	7/12	12/12	1.108	0.775

Group 1: subjects showing reproducible reverse-dipper in the first and second ABPM; Group 2: subjects showing reproducible dipper; Group 3: subjects showing reproducible non-dipper; Group 4: subjects who changed their initial pattern in the second ABPM; 24hSBP: 24-hour mean systolic blood pressure; 24hDBP: 24-hour mean diastolic blood pressure; dSBP: daytime mean systolic blood pressure; dDBP: daytime mean diastolic blood pressure; nSBP: nighttime mean systolic blood pressures; nDBP: nighttime mean diastolic blood pressure; CR: creatinine; TC: total cholesterol; TG: triglycerides; LDL-C: low density lipoprotein cholesterol; HDL-C: high density lipoprotein cholesterol; Lpa: lipoprotein A; FBG: fasting blood glucose; 2h PBG: 2 hours postprandial blood glucose; HbA1c: hemoglobin A1c; FT3: free triiodothyronine; FT4: free thyroxine; TSH: thyroid stimulating hormone; DM: diabetes mellitus. Compared with group 2, ^{**} $P < 0.01$; compared with group 3, ^{###} $P < 0.01$; compared with group 4, ^{△△} $P < 0.01$; compared with group 1, ^{▲▲} $P < 0.01$.

果之间存在矛盾冲突,可能是由于糖尿病^[10,11]、服用降压药时间^[8]、睡眠觉醒时间的定义^[12]、夜间行为^[13]和统计学方法^[6]等影响因素。例如,在糖尿病人群中,ND更常见、更具可重复性^[10,11];睡前加服降压药物比醒来服药者的ND发生率显著减小^[8];夜间小便的觉醒时间使D血压模式变模糊^[13];作为分类变量相比连续变量,夜间血压下降的长期可重复性稳定性较差^[6]。另外,老年高血压患者大多存在动脉粥样硬化和肾功能衰退等衰老性变化,对血压的调节力较低,血压变异性较大,因此血压昼夜节律的可重复性可能较年轻高血压患者低。本研究4组的糖尿病患病情况无显著性差异情况下,采用以下几种方法:保持睡眠觉醒时间和真实时间一致;服用降压药时间相对统一(发药时间为8:00am);剔除夜间小便后失眠的患者;把夜间血压下降分别作为分类变量和连续型变量来分析其可重复性等以尽量避免可能影响血压昼夜节律的因素。如表3可见,可重复的RD、D、ND模式两两之间的夜间收缩压有显著性差异,其他主要指标无明显差异($P < 0.001$),可见夜间血压是决定血压模式的主要因素;各组男女比例和HDL的差异可能是由于样本量偏小造成的偏差,因而本研究尚未发现可能影响血压模式重复性的因素。

综上所述,鉴于有些基于诊所或家庭血压测量的治疗措施可能过当,尤其是在高血压的诊断界值附近^[14],现临床上已将ABPM作为高血压诊断、治疗和预后评估的参考标准。虽然仅凭一次ABPM评估高血压平均水平和夜间血压模式等可重复性尚可,然而在开始抗高血压终生治疗以前应尽可能进行两次ABPM有助于制定更适宜的治疗方案,从而更早地达到治疗目标。

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