

· 临床研究 ·

老年人动态血压参数与轻度认知障碍的相关性

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【摘要】目的 探讨老年人动态血压参数与轻度认知障碍(MCI)的相关性。**方法** 选取2020年3月至7月于长海医院完成年度体检的306例离退休人员为研究对象, 收集人群一般资料、实验室检查及病史资料。采用便携式动态血压计记录各个时段平均血压、血压标准差、血压变异系数及晨峰血压、昼夜节律。使用蒙特利尔认知评估量表(MoCA)评估人群认知功能, 根据结果将人群分为轻度认知障碍(MCI)组(218例)和认知功能正常组(88例)。采用SPSS 26.0统计软件进行数据分析。根据数据类型, 分别采用t检验、Mann-Whitney U检验或 χ^2 检验进行组间比较。采用Spearman秩相关分析动态血压与MCI的相关性。采用多因素logistic回归模型分析MCI的影响因素。**结果** 与无认知障碍组比较, MCI组平均血压、血压标准差、血压变异系数及昼夜节律均显著增高, 差异有统计学意义($P<0.05$)。相关性分析结果显示, MoCA总分与24 h平均收缩压、白天平均收缩压、夜间平均收缩压、24 h平均收缩压标准差、白天平均收缩压标准差、夜间平均收缩压标准差、白天平均舒张压标准差、24 h平均收缩压变异系数、24 h平均舒张压变异系数、白天平均收缩压变异系数、夜间平均收缩压变异系数、夜间平均舒张压变异系数呈负相关($r=-0.151, -0.144, -0.136, -0.202, -0.253, -0.158, -0.253, -0.210, -0.190, -0.220, -0.178, -0.119; P<0.05$); 与24 h平均舒张压、白天平均舒张压、夜间平均舒张压呈正相关($r=0.163, 0.157, 0.138; P<0.05$)。多因素logistic回归分析结果显示, 年龄、24 h收缩压变异系数、昼夜节律中非杓型和反杓型($B=11.000, OR=1.115, P<0.01; B=0.270, OR=1.305, P<0.01; B=1.496, OR=4.646, P<0.01; B=1.306, OR=3.690, P<0.05$)是老年人发生MCI的独立危险因素。**结论** 老年人动态血压变异与MCI发生密切相关, 控制异常的血压变异可能有利于避免MCI的发生。

【关键词】 老年人; 血压变异性; 轻度认知障碍; 动态血压

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Correlation between parameters of ambulatory blood pressure and mild cognitive impairment in older adults

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【Abstract】 Objective To investigate the correlation between parameters of ambulatory blood pressure and mild cognitive impairment (MCI) among the elderly. **Methods** A total of 306 retired cadres who had finished the annual health examination at Shanghai Hospital from March to July in 2020 were enrolled as the research subjects. Their general data, results of laboratory tests, and medical history were collected. Portable ambulatory blood pressure monitor was used to record the average blood pressure, standard deviation of blood pressure, variation coefficient of blood pressure, morning blood pressure surge and circadian rhythm at the different time intervals. Montreal cognitive assessment (MoCA) was employed to evaluate the cognitive function. According to the results, the subjects were divided into MCI group ($n=218$) and the normal cognition group ($n=88$). SPSS statistics 26.0 was adopted for data analysis. Student's t test, Mann-Whitney U test, or Chi-square test was performed for intergroup comparison depending on data type. Spearman rank correlation analysis was conducted to analyze the correlation of ambulatory blood pressure and MCI. Multivariate logistic regression model was established to analyze the influencing factors for MCI. **Results** Compared with the normal cognition group, higher average blood pressure, standard deviation of blood pressure, variation coefficient of blood pressure, and circadian rhythm were observed in the MCI group ($P<0.05$). Correlation analysis indicated that the total MoCA score was negatively correlated with 24-hour mean systolic blood pressure, daytime mean systolic blood pressure, night mean systolic blood pressure, 24-hour mean systolic blood pressure standard deviation, daytime mean systolic blood pressure standard deviation, night mean systolic blood pressure standard deviation, daytime mean

diastolic blood pressure standard deviation, 24-hour mean systolic blood pressure coefficients of variation, 24-hour mean diastolic blood pressure coefficients of variation, daytime mean systolic blood pressure coefficients of variation, night mean systolic blood pressure coefficients of variation, and night mean diastolic blood pressure coefficients of variation ($r = -0.151, -0.144, -0.136, -0.202, -0.253, -0.158, -0.253, -0.210, -0.190, -0.220, -0.178, -0.119; P < 0.05$) , and positively correlated with 24-hour mean diastolic blood pressure, daytime mean diastolic blood pressure, and night mean diastolic blood pressure ($r = 0.163, 0.157, 0.138; P < 0.05$) . Multivariate logistic regression analysis showed that age, 24-hour mean systolic blood pressure coefficients of variation, non-dipper and reverse-dipper in the circadian rhythm ($B = 11.000, OR = 1.115, P < 0.01; B = 0.270, OR = 1.305, P < 0.01; B = 1.496, OR = 4.646, P < 0.01; B = 1.306, OR = 3.690, P < 0.05$) were independent risk factors for occurrence of MCI among the elderly.

Conclusion Ambulatory blood pressure variability is closely associated with the occurrence of MCI among the elderly. Controlling abnormal blood pressure variability may be beneficial in preventing the occurrence of MCI.

[Key words] aged; blood pressure variability; mild cognitive impairment; ambulatory blood pressure

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第七次人口普查数据显示我国60岁及以上老年人为2.64亿,65岁及以上人口为1.9亿,占总人口的13.5%。轻度认知障碍(mild cognitive impairment, MCI)是认知功能处于正常与痴呆间的一种过渡状态,65岁及以上人群患病率为10%~20%,超过一半的患者在5年内会进展为痴呆^[1]。血压产生一定范围内的波动称为“血压变异”(blood pressure variability, BPV)。近年有研究显示异常的BPV与靶器官损害密切相关,表现出心脑肾等重要器官结构和功能的异常^[2]。血压变异性加大可能是认知功能恶化的可改变的风险因素^[3]。本研究分析BPV与MCI的相关性,并进一步探讨老年人认知功能障碍的影响因素,为延缓MCI向老年痴呆过渡提供一定理论依据。

1 对象与方法

1.1 研究对象

选择2020年3月至7月于长海医院完成年度体检的306例离退休人员为研究对象,其中男性233例,女性73例;年龄60~96(76.61 ± 9.03)岁。纳入标准:(1)年龄≥60岁;(2)完成2020年度体检;(3)能配合完成蒙特利尔认知评估量表(Montreal cognitive assessment, MoCA);(4)自愿签署知情同意书。排除标准:(1)严重失语、失听及意识障碍、老年痴呆等不能配合流行病学调查;(2)恶性肿瘤;(3)严重肢体功能障碍;(4)未完成体检;(5)有精神疾病史。本研究经长海医院伦理委员会批准(编号:CHEC2020-114),所有研究对象或其家属知情同意并签署书面知情同意书。

1.2 方法

1.2.1 一般资料收集 采用横断面调查方法,由统一培训后的医护人员对所有对象进行面对面问卷调查,并收集体检数据。问卷调查的基本情况包括年龄、性别、体育锻炼、吸烟史、饮酒史、高血压病史、糖

尿病史、冠心病史及脑血管病史。体检内容包括身高、体质量、血常规、肝肾功能、血糖、糖化血红蛋白、总胆固醇、甘油三酯、低密度脂蛋白胆固醇及高密度脂蛋白胆固醇。

1.2.2 MCI评估 采用MoCA进行MCI评估,包括注意与集中、执行功能、记忆、语言、视空间结构技能、抽象思维、计算和定向力,其专门为筛查MCI而设计,在识别MCI时有较高的灵敏度和特异度^[4]。MoCA评分总分0~30分,<26分为存在认知功能障碍。根据评分结果,将研究对象分为MCI组(218例)和认知功能正常组(88例)。

1.2.3 24 h动态血压监测 采用国际验证合格的动态血压监护仪(型号TM2430)进行测量。根据《动态血压监测临床应用中国专家共识》^[5],尽可能确保监测时间>24 h,有效读数在设定读数的70%以上,设置6:00~22:00为日间时段,每30 min检测一次血压;22:00~6:00为夜间时段,每60 min检测一次血压。自动生成并记录以下动态血压参数数据:(1)24 h平均收缩压/舒张压(24-hour mean systolic blood pressure/24-hour mean diastolic blood pressure, 24hSBP/24hDBP)、日间平均收缩压/舒张压(daytime mean systolic blood pressure/daytime mean diastolic blood pressure, dSBP/dDBP)、夜间平均收缩压/舒张压(night mean systolic blood pressure/night mean diastolic blood pressure, nSBP/nDBP);(2)血压变异性指标:24 h平均收缩压标准差/舒张压标准差(24-hour mean systolic blood pressure standard deviation/24-hour mean diastolic blood pressure standard deviation, 24hSBP-SD/24hDBP-SD)、日间平均收缩压标准差/舒张压标准差(daytime mean systolic blood pressure standard deviation/daytime mean diastolic blood pressure standard deviation, dSBP-SD/dDBP-SD)、夜间平均收缩压标准差/舒张压标准差(night mean systolic blood pressure standard deviation/night mean diastolic blood

pressure standard deviation, nSBP-SD/nDBP-SD); 24 h 平均收缩压变异系数/舒张压变异系数(24-hour mean systolic blood pressure coefficients of variation/24-hour mean diastolic blood pressure coefficients of variation, 24hSBP-CV/24hDBP-CV)、日间平均收缩压变异系数/舒张压变异性系数(daytime mean systolic blood pressure coefficients of variation/daytime mean diastolic blood pressure coefficients of variation, dSBP-CV/dDBP-CV)、夜间平均收缩压变异性系数/舒张压变异系数(night mean systolic blood pressure coefficients of variation/night mean diastolic blood pressure coefficients of variation, nSBP-CV/nDBP-CV)。(3)晨峰血压增高:根据《老年人异常血压波动临床诊疗中国专家共识》^[6],起床后2 h 内的收缩压平均值减去夜间睡眠时收缩压最低值(夜间血压最低值前后共3次收缩压的平均值)≥35 mmHg(1 mmHg=0.133 kPa)。(4)血压昼夜节律分型:根据夜间血压下降率=(日间血压均值-夜间血压均值)×100%/日间血压均值,将血压昼夜节律分为以下几型:>20%为超勺型;10%~20%为勺型;0%~10%为非勺型;<0%为反勺型或夜间增高型。

1.3 统计学处理

采用SPSS 26.0统计软件进行数据分析。符合正态分布的计量资料以均数±标准差($\bar{x} \pm s$)表示,组

间比较采用t检验;不符合正态分布的计量资料使用中位数(四分位数间距)[$M(Q_1, Q_3)$]表示,组间比较采用Mann-Whitney U检验。计数资料以例数(百分率)表示,组间比较采用 χ^2 检验。采用Spearman秩相关分析动态血压与MCI的相关性。采用多因素logistic回归模型分析MCI的影响因素。 $P<0.05$ 为差异有统计学意义。

2 结 果

2.1 2组患者基线资料比较

与认知功能正常组比较,MCI组年龄、血尿素氮水平明显增高,且多有糖尿病史,锻炼少,差异有统计学意义($P<0.05$;表1)。

2.2 MOCA 总分与动态血压相关性分析

306例研究对象MOCA总分与24hSBP、dSBP、nSBP、24hSBP-SD、dSBP-SD、nSBP-SD、dDBP-SD、24hDBP-CV、24hDBP-CV、dSBP-CV、nSBP-CV、nDBP-CV呈负相关($r=-0.151, -0.144, -0.136, -0.202, -0.253, -0.158, -0.253, -0.210, -0.190, -0.220, -0.178, -0.119; P<0.05$);与24hDBP、dDBP、nDBP呈正相关($r=0.163, 0.157, 0.138; P<0.05$);与24hDBP-SD、nDBP-SD、dDBP-CV无相关性($P>0.05$)。

表1 2组患者基线资料比较

Table 1 Comparison of baseline data between two groups

Item	Normal cognition group ($n=88$)	MCI group ($n=218$)	$t/Z/\chi^2$	P value
Age[years, $M(Q_1, Q_3)$]	69.5(66.0,75.0)	79.0(71.0,87.0)	-6.635	<0.01
Gender[n(%)]			3.168	0.075
Male	61(69.3)	172(78.9)		
Female	27(30.7)	46(21.1)		
BMI(kg/m^2 , $\bar{x} \pm s$)	24.58±3.00	24.92±2.72	-0.958	0.339
Smoking[n(%)]	81(92.0)	187(85.8)	2.263	0.133
Alcohol drinking[n(%)]	61(69.3)	149(68.3)	0.027	0.869
Physical exercise[n(%)]	80(90.9)	164(75.2)	9.540	0.002
Hypertension[n(%)]	64(72.7)	162(74.3)	0.082	0.775
Diabetes mellitus[n(%)]	15(17.0)	64(29.4)	4.962	0.026
Atrial fibrillation[n(%)]	5(5.7)	27(12.4)	3.009	0.083
Cerebral apoplexy	12(13.6)	35(16.1)	0.228	0.595
TBIL[mmol/L , $M(Q_1, Q_3)$]	12.9(10.0,17.1)	12.7(10.4,16.0)	-0.445	0.656
SCr[$\mu\text{mol}/\text{L}$, $M(Q_1, Q_3)$]	79.0(69.0,89.0)	81.0(70.3,96.0)	-1.248	0.212
BUN[mmol/L , $M(Q_1, Q_3)$]	5.2(4.5,6.1)	5.7(4.8,6.5)	-2.691	0.007
UA[$\mu\text{mol}/\text{L}$, $M(Q_1, Q_3)$]	333.0(282.5,388.0)	337.0(294.5,402.5)	-1.043	0.297
FBG[mmol/L , $M(Q_1, Q_3)$]	5.8(5.4,6.5)	5.8(5.4,6.6)	-1.032	0.302
HbA1c[%, $M(Q_1, Q_3)$]	5.9(5.6,6.3)	5.9(5.6,6.5)	-1.128	0.259
TG[mmol/L , $M(Q_1, Q_3)$]	1.4(1.0,1.7)	1.3(0.9,1.8)	-0.249	0.803
TC[mmol/L , $M(Q_1, Q_3)$]	4.5(3.8,5.2)	4.3(3.7,5.1)	-0.984	0.325
HDL-C[mmol/L , $M(Q_1, Q_3)$]	1.3(1.1,1.6)	1.3(1.1,1.5)	-0.643	0.520
LDL-C[mmol/L , $M(Q_1, Q_3)$]	2.9(2.3,3.5)	2.8(2.1,3.3)	-1.748	0.081

BMI: body mass index; TBIL: total bilirubin; SCr: serum creatinine; BUN: blood urea nitrogen; UA: uric acid; FBG: fasting blood glucose; HbA1c: glycosylated hemoglobin A1c; TG: triglycerides; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol。

2.3 2组患者动态血压比较

与认知功能正常组比较,MCI组24 h平均收缩压、夜间平均收缩压、24 h平均舒张压、日间平均舒张压、各个阶段血压标准差、各个阶段血压变异系数均明显增高,差异有统计学意义($P<0.05$);余动态血压参数2组患者间差异无统计学意义(表2)。

2.4 2组昼夜节律和晨峰血压比较

与认知功能正常组比较,MCI组异常节律明显增多,差异有统计学意义($P<0.05$);2组患者晨峰血压比较,差异无统计学意义(表3)。

2.5 多因素 logistic 回归分析 MCI 的影响因素

以是否发生认知轻度障碍(发生=1,未发生=0)为二项分类的因变量,以年龄、是否参加锻炼(是=1,无=0)、糖尿病史(有=1,无=0)、尿素氮水平、24hSBP、24hSBP-SD、24SBP-CV、昼夜节律(1=杓型血压,2=非杓型血压,3=反杓型血压,4=超杓型血压)、晨峰血压为自变量,纳入多因素 logistic 回归模型,采用向前条件筛选协变量。结果显示年龄、24hSBP-CV 及昼夜节律异常是发生轻度认知障碍的独立危险因素($P<0.05$;表4)。

表2 2组患者动态血压比较

Table 2 Comparison of ambulatory blood pressure between two groups

($\bar{x}\pm s$)

Item	Normal cognition group ($n=88$)	MCI group ($n=218$)	t	P value
24hSBP	126.11±12.69	129.54±13.02	-2.097	0.037
dSBP	128.02±13.50	131.28±13.59	-1.899	0.058
nSBP	120.94±13.34	125.10±15.69	-2.187	0.030
24hDBP	74.26±7.84	72.10±7.13	2.336	0.020
dDBP	75.73±8.24	73.43±7.53	2.349	0.019
nDBP	70.10±8.70	68.71±8.12	1.333	0.183
24hSBP-SD	14.38±3.85	16.80±4.18	-4.690	<0.01
24hDBP-SD	9.44±2.63	10.13±2.68	-2.028	0.043
dSBP-SD	13.97±4.07	16.64±4.11	-5.166	<0.001
nSBP-SD	11.67±3.70	13.24±4.14	-3.237	0.001
dDBP-SD	9.07±3.04	9.89±2.82	-2.247	0.025
nDBP-SD	7.85±2.50	8.56±2.85	-2.046	0.042
24hSBP-CV	11.38±2.68	13.06±2.99	-4.583	<0.01
24hDBP-CV	12.76±3.45	14.14±3.43	-3.183	0.002
dSBP-CV	10.90±2.89	12.78±3.08	-4.909	<0.01
nSBP-CV	9.71±2.99	10.60±3.33	-2.163	0.031
dDBP-CV	12.02±4.00	13.55±3.58	-3.256	0.010
nDBP-CV	11.29±3.67	12.55±3.98	-2.555	0.011

24hSBP: 24-hour mean systolic blood pressure; dSBP: daytime mean systolic blood pressure; nSBP: night mean systolic blood pressure; 24hDBP: 24-hour mean diastolic blood pressure; dDBP: daytime mean diastolic blood pressure; nDBP: night mean diastolic blood pressure; 24hSBP-SD: 24-hour mean systolic blood pressure standard deviation; 24hDBP-SD: 24-hour mean diastolic blood pressure standard deviation; dSBP-SD: daytime mean systolic blood pressure standard deviation; nSBP-SD: night mean systolic blood pressure standard deviation; dDBP-SD: daytime mean diastolic blood pressure standard deviation; nDBP-SD: night mean diastolic blood pressure standard deviation; 24hSBP-CV: 24-hour mean systolic blood pressure coefficients of variation; 24hDBP-CV: 24-hour mean diastolic blood pressure coefficients of variation; dSBP-CV: daytime mean systolic blood pressure coefficients of variation; nSBP-CV: night mean systolic blood pressure coefficients of variation; dDBP-CV: daytime mean diastolic blood pressure coefficients of variation; nDBP-CV: night mean diastolic blood pressure coefficients of variation。

表3 2组患者昼夜节律和晨峰血压比较

Table 3 Comparison of circadian rhythm and morning blood pressure surge between two groups

Group	n	Circadian rhythm (n)				Morning blood pressure surge (mmHg)
		Dippers	Non-dippers	Inverse dippers	Extreme dippers	
Normal cognition	88	32	34	22	0	29.0(19.3,35.8)
MCI	218	48	93	68	9	30.0(20.0,39.0)
χ^2/Z		9.630				-0.741
P value		0.022				0.459

1 mmHg=0.133 kPa.

表4 多因素 logistic 回归分析 MCI 的影响因素

Table 4 Multivariate logistic regression analysis on influencing factors of MCI

Factor	B	SE	Wald χ ²	OR(95%CI)	P value
Age	11.000	0.020	30.409	1.115(1.073–1.160)	<0.01
24hSBP-CV	0.270	0.674	15.802	1.305(1.145–1.488)	<0.01
Circadian rhythm(non-dipper)	1.496	0.381	15.383	4.464(2.114–9.427)	<0.01
Circadian rhythm(reverse-dipper)	1.306	0.414	9.926	3.690(1.638–8.314)	0.002

MCI: mild cognitive impairment; 24hSBP-CV: 24-hour mean systolic blood pressure coefficients of variation.

3 讨 论

本世纪中叶,我国老年人口将超4亿,随着人口老龄化加剧,老年认知功能障碍的患者也越来越多。随着年龄逐渐增大,老年人认知功能逐渐下降,从轻度认知障碍最终发展为老年痴呆。因此寻找MCI的有效预测因子及可控的危险因素,及早对MCI进行干预,对延缓痴呆的发生至关重要。

本研究结果显示,MCI组年龄、血尿素氮水平明显高于正常组,不参加健身锻炼、有糖尿病史老年人患MCI比例增多,提示年龄、血尿素氮水平、健身锻炼、糖尿病史与MCI关系密切。年龄是已知认知障碍发生非常重要的影响因素,研究发现,60~64岁人群MCI患病率为6.7%,65~69岁为8.4%,70~74岁为10.1%,75~79岁为14.8%,80~84岁为25.2%^[7]。研究显示规律的体育锻炼有助于减轻MCI患者认知功能的恶化^[8]。

血压变异是人类血压最基本的生理特征之一,老年人容易发生血压波动幅度和频率的非生理性变化,称为异常血压波动。研究显示高血压与脑血管疾病和认知障碍密切相关,高血压可导致脑小血管低灌注、氧化应激、自身调节损伤、血脑屏障和脑淀粉样血管病,随着时间的推移,尤其是血压控制不佳时可能导致认知功能恶化^[9]。然而即使在血压控制良好的老年人中,较高的血压变异性(而不是血压平均动态血压)亦与认知障碍相关^[10]。本研究结果显示,动态血压、动态血压标准差及动态血压变异系数与MCI相关,而多因素logistic回归结果显示24hSBP-CV是MCI的独立危险因素。丁雯等^[11]meta分析结果发现,认知障碍组24hSBP-CV明显高于非认知障碍组。Fujiwara等^[12]研究也表明动态血压变异性增高与认知障碍相关。Zhang等^[13]在一项中国社区前瞻性队列研究中,分析7874例年龄≥60岁的老年人血压对认知功能下降的影响,结果表明收缩压升高、舒张压降低、平均动脉压降低及脉

压升高加速了老年人认知功能下降的速度。此外,强化降压可以减缓MCI、痴呆及脑白质损害的发展^[14]。BPV导致MCI的机制尚不明确,可能长期的BPV导致严重脑动脉粥样硬化继发的脑灌注不足,血流动力学不稳定^[15];BPV与脑血管反应性降低有关,而脑血管反应性降低将导致脑血管功能障碍^[16]。另外血压变异性增加也与白质高信号和脑萎缩显著相关,即使校正血压水平和其他混杂因素后,老年人仍易患痴呆、抑郁和跌倒^[17]。以上机制可能使脑组织缺氧损伤加重,从而导致认知功能的神经元细胞受损害,最终发展为认知障碍。

老年人异常BPV还表现为血压昼夜节律的异常改变和晨峰血压增高。本研究结果显示MCI组昼夜节律异常比认知功能正常组明显增多,并且是MCI的独立危险因素,与国外文献研究结果一致。史静静等^[18]研究显示老年人血压昼夜节律异常是认知障碍的危险因素,与平均血压无关。邵胜等^[19]探讨高龄(≥80岁)高血压患者血压昼夜节律改变与认知功能的关系,结果显示血压节律异常的高龄老年高血压患者较血压节律正常者更容易发生认知功能损害,并且不同的昼夜节律类型在认知评估内容(包括定向力、记忆力、注意力和计算力、回忆力方面)影响不同。Pillai等^[20]研究发现昼夜节律异常伴随着脑脊液和血浆中体液免疫应答的改变及神经退行性变的脑脊液生物标志物的改变,导致免疫循环标志物的异常和炎性相关认知功能减退。本研究未发现血压晨峰与MCI有相关性,与丁雯等^[11]meta分析结果一致。但也有文献报道老年人血压晨峰增高与认知障碍相关,是认知能力下降的危险因素^[21]。

综上,老年人BPV与MCI发生密切相关,老年人应该积极监测动态血压,采取积极有效的措施控制异常BPV,从而延缓认知功能损害的发生与发展。

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