Nocturnal Blood Pressure Rise as A Predictor of Cognitive Impairment Among the Elderly: A Retrospective Cohort Study

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Abstract

Background: This study investigated the relationship between ambulatory blood pressure monitoring (ABPM), cognitive function and cerebral Magnetic Resonance Imaging (MRI) among elderly patients to assess effective hypertension management for preventing the progression of cognitive impairment.

Methods: Participants comprised 305 elderly patients aged ≥ 65 years, who were divided into the cognitive impairment group (CI, $n=130$), and the non-cognitive impairment group (NCI, $n=175$), according to MMSE score. All participants underwent ABPM for the evaluation of possible hypertensive disorder and cerebral MRI for the evaluation of cerebral small vessel disease. Follow-up was performed by telephone or medical records.

Results: Of the 305 participants, 130 (42.6%) were identified with cognitive impairment (CI), with the average systolic blood pressure (BP) of 127 mmHg and diastolic BP of 66 mmHg. According to ABPM, only 13.1% had dipper pattern, 45.6% had nocturnal BP rise, while 41.3% had non-dipper pattern. Compared with NCI patients, the CI group had significantly higher night-time systolic BP (130.0 ± 18.2 vs. 123.9 ± 15.1 , $p=0.011$), and more participants had nocturnal BP rise (52.3% vs. 40.6%, $p=0.042$). Nocturnal BP rise was associated with greater white matter hyperintensities (WMH) ($p=0.013$). After 2.03 years of follow-up, there were 35 all-cause deaths, and 33 cases of major adverse cardiac and cerebrovascular events (MACCE). CI was independently associated with all-cause mortality during long-term observation ($p<0.01$). Nocturnal BP rise had no significant predictive ability for all-cause mortality in the elderly patients ($p=0.178$).

Conclusions: Nocturnal BP rise contributed to greater WMH volumes and cognitive impairment in the elderly patients. To prevent the progression of cognitive dysfunction, it is critical to control BP based on ABPM.

Background

Dementia affects approximately 50 million people worldwide, and is expected to increase by nearly 9.9 million new cases each year. While Alzheimer's disease is the leading cause of cognitive impairment (CI), vascular dementia is the second leading cause, with no effective therapies⁽¹⁾. Cerebral small vessel disease is the most common pathology underlying vascular dementia, including lacunar infarcts (LCI) or white matter hyperintensities (WMH)⁽²⁾. Hypertension can affect brain structure and function, which is known to be associated with CI. It is the major vascular risk factor for CI⁽³⁾. If hypertension is properly controlled, it could potentially stave off the onset of cognitive deficits.

The associations between blood pressure (BP) and brain health are complex, and are dependent on many factors such as age, hypertension chronicity and hypertension variation. The elevated BP in midlife, particularly untreated hypertension, increases the risk for CI. Studies have either failed to find any association between hypertension and CI in the eighth, ninth and tenth decade of life or have found high

BP to be protective against CI⁽³⁾. Systolic and diastolic BP were positively correlated with WMH grade, and higher night-time systolic BP levels were found to contribute to greater WMH volumes in elderly hypertensive patients⁽⁴⁾. However, the relationship between blood pressure variation (BPV) and CI has not been extensively investigated, and previous studies have yielded conflicting results.

The present study was undertaken to assess the associations between BPV and CI, and investigate the value of BPV to predict the mortality in elderly patients.

Methods

Participants

This study included 583 inpatients, ≥ 65 years age, who received cognitive assessment and cerebral MRI at the Geriatric Medicine department of the Beijing Friendship Hospital between January 2014 and September 2019. The participants were followed-up until March 2020. Among these subjects, three were excluded for chronic kidney disease, 57 and 165 were excluded for incomplete clinical examination and ambulatory blood pressure monitoring (ABPM), respectively, and 16 were excluded for missed follow-up. Finally, 305 participants were included in this analysis to assess the effect of BPV and its risk factors on cognitive function in the elderly subjects (Figure 1).

The study was approved by the ethics committee of Beijing Friendship Hospital, Capital Medical University (code: 2018-P2–120-01), and was conducted in accordance with the Declaration of Helsinki.

Demographic characteristics, including years of education, medical history, clinical information and concurrent medications, were collected.

Hypertension was defined as systolic blood pressure (SBP) ≥ 140 mmHg, diastolic blood pressure (DBP) ≥ 90 mmHg or ongoing therapy for hypertension. Type-2 diabetes was defined as glycosylated hemoglobin (HbA1c) $\geq 6.5\%$, a non-fasting plasma glucose concentration ≥ 200 mg/dL, fasting plasma glucose concentration ≥ 126 mg/dL, or if the patient was treated with oral hypoglycemic medications or insulin.

Laboratory measurements

Lipids, including total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C), were measured using standard methods of the central laboratory of the Beijing Friendship Hospital. Fasting glucose, glycosylated hemoglobin (HbA1c), liver and renal function, and albumin (ALB) were also measured. Estimated glomerular filtration rate (EGFR) was calculated by EPI equation.

Ambulatory Blood Pressure Monitoring

A validated ambulatory recorder (DMS-ABP, USA) and cuff were used on the non-dominant arm to perform ABPM. BP was measured at 30-min intervals for day (06.00–21.59 hours) and 1-h intervals for night (22.00–05.59 hours). BP, including 24-h mean value, mean daytime value and mean night-time value, were calculated from recorded measurements and used in data analyses.

The nocturnal BP fall (%) was calculated as: (daytime SBP–night-time SBP)/daytime SBP. We classified the nocturnal BP fall into the following three patterns: the dipper pattern, if the nocturnal BP fall was >10%; the non-dipper pattern, if it was between 0% and 10%; and the rise pattern, if it was <0%. Patients with an extreme dipper pattern (nocturnal BP fall >20%) were combined with those with the dipper pattern due to the limited number of cases (n =6). Nocturnal hypertension was defined as a night-time SBP $\geq$ 120 mmHg and/or night-time DBP $\geq$ 70 mmHg, based on the 2014 guidelines for the management of hypertension published by The Japanese Society of Hypertension.

Magnetic Resonance Imaging protocol and assessments

MRI images were acquired using a 3.0 T scanner (Siemens, Berlin, Germany) in the Radiology Department of our hospital. Sequences included T2-weighted imaging (T2WI), T1-weighted imaging (T1WI), diffusion-weighted imaging (DWI), fluid-attenuated inversion recovery imaging (FLAIR) and susceptibility-weighted imaging (SWI). The main parameters were as follows: repetition time (TR) = 4,500 ms, echo time (TE) = 84 ms, flip angle (FA) = 120°, matrix = 256 *256, field of view (FOV) = 220 * 220 mm², slice thickness = 5 mm, and slice gap = 1 mm, number of slices = 24.

White matter hyperintensities (WMHs) were identified as hyperintense areas in the periventricular and deep white matter on both T2WI and FLAIR. WMH was rated using the Fazekas scale on FLAIR images. Lacunar infarcts (LACs) were defined as small (diameter of 3-15 mm), sharply demarcated hyperintense lesions on T2WI with corresponding foci of FLAIR low signal intensity and assessed in the basal ganglia, internal capsule, thalamus, brainstem, radiating crown, semioval center. The number of WMHs and LCIs were calculated to assess the severity of cerebral small vessel disease. MRI assessments were performed by two experienced neuroradiologists who were blinded to the clinical information.

Measurement of cognition

Cognitive function was assessed by the Mini Mental Status Examination (MMSE) and the Montreal Cognitive Assessment (MoCA). MMSE is a brief examination of CI, which is used as a functional method for assessing cognitive function. It has 11 items with a total score 0–30, and <27 score is indicative of CI. MoCA assesses the following functions: executive functions (5 points), name (3 points), memory (5 points), concentration (6 points), language (3 points), conceptual thinking (2 points), and orientation (6 points).

Follow-up was performed by reviewing data in medical records or by telephone interviews. The primary outcome was all-cause mortality. Secondary endpoints were major adverse cardiac and cerebrovascular

events (MACCE), including acute coronary syndrome (acute myocardial infarction or unstable angina pectoris), heart failure of NYHA III-IV, stroke/transient ischemic attacks (TIA) and cerebral hemorrhage.

Statistical analysis

All continuous variables were reported as mean $\pm$ standard deviation ($M \pm SD$), and categorical variables were presented as counts and percentages. The Kolmogorov–Smirnov test was used for the normality assumption. Pearson's chi-squared test was used to investigate the categorical variables. For the analyses of continuous variables with normal distribution, t-test was used for examining the differences between two groups. Kruskal–Wallis with post hoc Mann–Whitney U-test was used to analyze the continuous variables that could not be transformed to normal distribution. Correlations between nocturnal BP fall and MMSE or MoCA were evaluated using the linear regression. The multinomial logistic regression was employed to assess the association between nocturnal BP rise and specific cognitive domains. Cox regression and Kaplan–Meier curves were used for survival analysis. All statistical analyses were performed using SPSS statistical software version 24.0 for Windows (SPSS Inc.), and a p-value < 0.05 was considered statistically significant.

Results

Baseline characteristics of participants

A total of 305 participants were included in the study. The mean age was 81 years, the average years of education received was 14, 69% of participants were men, the average BMI was 24, 10.2% were smokers, 79% had hypertension, and 39.3% had diabetes. As shown in Table 1, 35.7% of subjects were taking anti-platelet therapy, 46.5% were on a statin, 41.3% were on an ACEI or ARB, 43% were on a CCB, and 30.2% were taking a beta-blocker. The average HbA1c was 6.1%. The average TC was 4.0 mmol/l, TG was 1.3 mmol/l, and LDL-C was 2.4 mmol/l.

Of the 305 participants, 42.6% were identified as having CI with MMSE scores < 27 . Subjects with (CI group, $n = 130$) and without CI (NCI group, $n = 175$) were compared according to demographic and clinical characteristics, and risk factors. As shown in Table 1, compared to NCI subjects, subjects with CI were significantly older (82.5 ± 7.7 vs. 79.1 ± 7.3 years, $p < 0.001$), less educated (13.0 ± 4.0 vs. 14.8 ± 3.0 years, $p < 0.001$), had higher fasting glucose (6.1 ± 2.3 vs. 5.5 ± 1.3 mmol/l, $p = 0.016$), lower HgB (127.6 ± 16.3 vs. 132.0 ± 15.0 g/dl, $p = 0.015$), significantly lower ALB (36.2 ± 4.5 vs. 38.5 ± 4.3 g/dl, $p < 0.001$), significantly lower eGFR (72.1 vs. 79.2 ml/min/1.73 m², $p < 0.001$), and more severe WMH (2 vs. 1, $p < 0.01$) and LCI (1.88 ± 0.81 vs. 1.52 ± 0.71 , $p = 0.019$).

After an average follow-up of 2.03 ± 1.45 years, there were 35 all-cause deaths. Among them, 21 patients died due to pneumonia or abdominal infection, four due to cancer, four due to cardiovascular disease, and six due to other diseases. A total of 33 cases suffered from MACCE. Among them, 21 patients had stroke/TIA or cerebral hemorrhage, with 12 cases of acute coronary syndrome or acute heart failure.

Table 1
Demographic characteristics of the study population

	All subjects (N = 305)	NCl group (n = 175)	Cl group (n = 130)	p-value
Age, years	80.6 ± 7.6	79.1 ± 7.3	82.5 ± 7.7	< 0.001*
Male, n (%)	210(69)	125 (71.4)	85(65.4)	0.260
Education, years	14.0 ± 3.6	14.8 ± 3.0	13.0 ± 4.0	< 0.001*
BMI, kg/m ²	24.3 ± 3.6	24.5 ± 3.6	23.9 ± 3.6	0.150
Smoking, n (%)	31 (10.2)	17(9.8)	14 (10.8)	0.124
Hypertension, n (%)	242(79)	136 (77.7)	106 (81.5)	0.415
Diabetes, n (%)	120 (39.3)	67(38.3)	53 (40.8)	0.661
FG, mmol/L	5.7 ± 1.8	5.5 ± 1.3	6.1 ± 2.3	0.016*
HgB	130.1 ± 15.7	132.0 ± 15.0	127.6 ± 16.3	0.015*
ALB	37.5 ± 4.5	38.5 ± 4.3	36.2 ± 4.5	< 0.001*
HbA1c, %	6.1 ± 1.6	5.9 ± 1.0	6.0 ± 1.1	0.168
Cr, mmol/l	75.5 (25.2-205.4)	73.5 (25.5-166.9)	79.8 (34.8-205.4)	0.021*
eGFR, ml/min/1.73 m ²	77.7 (17.3-113.9)	79.2 (32.6-113.9)	72.1 (17.3-101.8)	< 0.001*
TC, mmol/L	4.0 ± 1.1	4.0 ± 0.9	4.1 ± 1.3	0.541
TG, mg/dL	1.3 ± 0.8	1.3 ± 0.9	1.2 ± 0.7	0.638
HDL-C, mg/dL	1.2 ± 0.3	1.2 ± 0.3	1.1 ± 0.3	0.634
LDL-C, mg/dL	2.4 ± 0.8	2.4 ± 0.7	2.4 ± 1.0	0.478
Antiplatelet, n (%)	109 (35.7)	62 (35.4)	47 (36.2)	0.896
Statin, n (%)	151 (46.5)	93 (53.1)	58 (44.6)	0.141
ACEI/ARB, n (%)	126 (41.3)	72 (41.1)	54 (41.5)	0.945
CCB, n (%)	263 (43)	69 (39.4)	52 (40)	0.920
beta-blocker, n (%)	92 (30.2)	54 (30.9)	38(29.2)	0.760
WMH	2(0–3)	1(0–3)	2(0–3)	< 0.001*
LCI	1.64 ± 2.66	1.52 ± 0.71	1.88 ± 0.81	0.019*

	All subjects (N = 305)	NCl group (n = 175)	CI group (n = 130)	p-value
MoCA	21.64 ± 6.14	25.58 ± 3.11	16.33 ± 5.13	< 0.001*
MMSE	25.55 ± 4.81	28.66 ± 1.05	21.36 ± 4.72	< 0.001*

Values are mean ± SD, n (%), or median (interquartile range). BMI, body mass index; FG, Fasting glucose; HgB, hemoglobin; ALB, albumin; HbA1c, hemoglobin A1c; Cr, Creatinine; eGFR, estimated Glomerular Filtration Rate; TC, Total cholesterol; TG, Triglycerides; HDL-C, high-density lipoprotein; LDL-C, low-density lipoprotein; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; WMH, white matter hyperintensities; LCI, Lacunar cerebral infarction; MoCA, Montreal Cognitive Assessment; MMSE, Mini Mental Status Examination

Bp Variation And Cognitive Impairment

BP was reasonably controlled, with an average SBP of 127 mmHg and DBP of 66 mmHg. According to ABPM, 13.1% of patients had dipper pattern, 45.6% had nocturnal BP rise, and 41.3% had non-dipper pattern. Compared with NCI patients, the patients with CI had significantly higher night-time SBP (130.0 ± 18.2 mmHg vs. 123.9 ± 15.1 mmHg, $p = 0.011$), and more patients had nocturnal BP rise (52.3% vs. 40.6%, $p = 0.042$). In contrast, there was no significant inter-group difference in DBP. The incidence of daytime SBP and nocturnal hypertension was higher in the patients with CI than those with normal cognition, but the difference was not significant (Table 2). Nocturnal BP fall had a positive correlation with MMSE ($R^2 = 0.037$, $p = 0.001$) and MoCA ($R^2 = 0.028$, $p = 0.004$) (Fig. 2).

Table 2
Ambulatory blood pressure monitoring parameters according to the cognitive function

	All subjects (n = 305)	NCI (n = 175)	CI (n = 130)	p-value
Mean SBP, mmHg	127.4 ± 13.8	126.1 ± 12.5	129.2 ± 15.2	0.055
Mean DBP, mmHg	66 ± 8.5	65.9 ± 8.1	66.1 ± 9.0	0.887
dSBP, mmHg	127.1 ± 14.1	125.9 ± 13.2	128.7 ± 15.1	0.104
dDBP, mmHg	66.1 ± 8.7	66.1 ± 8.3	66.0 ± 9.1	0.908
nSBP, mmHg	126.5 ± 16.7	123.9 ± 15.1	130.0 ± 18.2	0.002*
nDBP, mmHg	64.4 ± 9.9	63.6 ± 9.3	65.5 ± 10.6	0.114
Nocturnal hypertension, n(%)	207(67.9)	112(64)	95(73.1)	0.093
BP category				
Dipper, n(%)	40(13.1)	24(13.8)	16(12.3)	0.719
Non-dipper, n(%)	126(41.3)	80(45.7)	46(35.4)	0.070
Rise, n(%)	139(45.6)	71(40.6)	68(52.3)	0.042*

SBP, systolic blood pressure; DBP, diastolic blood pressure; CI, cognitive impairment; NCI, non-cognitive impairment. *, $p < 0.05$.

The elderly patients with nocturnal BP rise had memory loss (1.78 ± 1.78 vs. 2.33 ± 1.70 , $p = 0.007$), less concentration (3.89 ± 1.84 vs. 4.55 ± 1.63 , $p = 0.001$), lower conceptual thinking (1.31 ± 0.80 vs. 1.49 ± 0.73 , $p = 0.042$), and less orientation (5.15 ± 1.42 vs. 5.58 ± 1.02 , $p = 0.003$) than those without nocturnal BP rise. There were significantly more WMH locations in the nocturnal BP rise group than in those without nocturnal BP rise (1.77 ± 0.80 vs. 1.59 ± 0.74 , $p = 0.042$) (Table 3).

Table 3
Relationship between neuropsychological test results and nocturnal BP rise

	Nocturnal BP Rise (n = 139)	Nocturnal BP Non-rise (n = 166)	p-value
Executive functions	3.32 ± 1.49	3.60 ± 1.41	0.102
Name	2.60 ± 0.75	2.67 ± 0.66	0.424
Memory	1.78 ± 1.78	2.33 ± 1.70	0.007*
Concentration	3.89 ± 1.84	4.55 ± 1.63	0.001*
Language	2.04 ± 1.05	2.21 ± 0.92	0.121
Conceptual thinking	1.31 ± 0.80	1.49 ± 0.73	0.042*
Orientation	5.15 ± 1.42	5.58 ± 1.02	0.003*
MoCA	20.45 ± 6.54	22.63 ± 5.62	0.002*
MMSE	24.51 ± 5.69	26.42 ± 3.73	0.001*
WHM	1.77 ± 0.80	1.59 ± 0.74	0.042*
LCI	1.64 ± 2.57	1.54 ± 2.65	0.760

MMSE, Mini Mental Status Examination; MoCA, Montreal Cognitive Assessment; WMH, white matter hyperintensities; LCI, Lacunar cerebral infarction; *, $p < 0.05$

Nocturnal BP rise was correlated with increased risk of disorientation (95% CI, 0.748(0.616–0.909), $p = 0.003$), lower conceptual thinking (95% CI, 0.736(0.546–0.990), $p = 0.043$), less concentration (95% CI, 0.806(0.706–0.919), $p = 0.001$), and memory loss (95% CI, 0.836(0.733–0.954), $p = 0.008$). After adjustment for age and gender, nocturnal BP rise significantly increased the risk of disorientation (95% CI, 0.801(0.653–0.982), $p = 0.033$), lower conceptual thinking (95% CI, 0.698(0.504–0.965), $p = 0.030$), and less concentration (95% CI, 0.846(0.735–0.974), $p = 0.020$) (Fig. 3).

According to the Cox regression models, CI was independently associated with all-cause mortality during long-term observation ($p < 0.01$), with 499% increase during follow-up. Nocturnal BP rise had no significant predictive value for all-cause mortality in the elderly patients (C-statistic = 0.178, 95% CI, 0.432–0.579) (Fig. 4).

Discussion

Cognitive impairment (CI) is rampant among the elderly worldwide. This study enrolled 305 cases, with a mean SBP of 127.4 mmHg and DBP of 66 mmHg. Among them 130 (42.6%) participants were identified with CI. They had worse nutrition and kidney function than individuals with normal cognition, which had a negative effect on the life quality and long-term prognosis. Hypertension is a major risk factor for

cognitive dysfunction^(4, 5), and the results of Honolulu Asia Aging Study demonstrated a positive association between lower brain volume, neuritic plaques, and hypertension ⁽⁵⁾. However, the relationship between BP variation and cognitive function was not known.

This study demonstrated that in elderly patients (mean age of 81 years), night-time SBP and nocturnal BP rise were positively correlated with CI, even if the patients had normal BP. Mean BP and daytime BP showed no correlation. Nocturnal hypertension was not significantly higher in the CI group. These results are consistent with the findings of Manabu Kokubo and his colleagues ⁽⁴⁾, who reported that higher night-time SBP levels contributed to greater WMH volumes in elderly hypertensive patients. High nocturnal BP is also associated with an increase in cardiovascular events ⁽⁶⁾, as well as the onset of chronic kidney disease ⁽⁷⁾.

Despite enormous evidence supporting the role of atherosclerosis in the pathogenesis and progression of CI, the mechanistic relationship between nocturnal BP and CI remains unknown. Some possible mechanisms are as follows. First, nocturnal BP rise decreased cerebral blood flow, and was related to higher levels of insulin resistance markers in normotensive and untreated mildly hypertensive adults ⁽⁸⁾. Second, non-dipping of nocturnal BP increased the markers of endothelial dysfunction and inflammation, which are proposed to be a candidate mechanism of atherosclerosis ⁽⁹⁾. Moreover, cerebral small vessel disease including LCI and WMH, played a major role in the senile vascular CI ^(2, 10). This study also demonstrated that elderly patients with CI had more severe WMH and LCI than those without CI. Nocturnal BP rise contributed to greater WMH volumes, but not LCI. This may be because WMH is more sensitive to the atherosclerotic risk factor than LCI.

Although several studies have suggested that the impact of hypertension on cognition is global, not all studies broadly investigated the distinct cognitive domains. Some studies showed that cognitive domains that are most vulnerable to hypertension are attention and executive functioning domains ⁽¹¹⁾, since cognitive processes rely heavily on the integrity of frontal and subcortical brain structures, which may be most vulnerable to the effects of hypertension. We observed an association between nocturnal BP rise and decline in orientation, conceptual thinking and concentration, but not in declarative executive function and memory ⁽¹²⁾. Nocturnal BP rise could decrease orientation by 19.9%, conceptual thinking by 30.2%, and concentration by 15.4%, after adjustment for age and gender. This finding supported our hypothesis that the deterioration of orientation, conceptual thinking and concentration with aging is a BP variation-related impairment ⁽¹³⁾. Some studies reported that processing speed is the first cognitive domain to be impacted by white matter lesion burdens due to uncontrolled hypertension. Heidi I L Jacobs revealed that WMH location influenced the relation between WMH and executive functioning, and parietal WMH are a significant contributor to executive decline in MCI ⁽¹⁴⁾. This study did not assess the WMH location in detail.

The present study showed that baseline CI measured by MMSE score was associated with an elevated risk of all-cause mortality, which was consistent with the results of previous studies ^(15, 16). However, the

prognostic value of the nocturnal BP rise has not been established. The Ambulatory Blood Pressure Collaboration in Patients With Hypertension (ABC-H) examined this issue in a meta-analysis of 17312 hypertensive patients (mean age of 50–70 years), who were followed-up for 4–8 years. They found that the non-dipping pattern could predict 33% of all-cause mortality and 57% of cardiovascular mortality, after adjustment for 24-hour SBP. Among the four different dipping subgroups, patients with nocturnal BP rise had the worst prognosis for cardiovascular events and all-cause mortality, and nocturnal BP rise was responsible for most of the non-dipping pattern adverse prognosis⁽¹³⁾. This study showed that the patients with nocturnal BP rise had higher incidence of cardiovascular disease than those without nocturnal BP rise (15.1% vs. 7.2%, $p = 0.027$). However, nocturnal BP rise was not significantly associated with all-cause mortality. Perhaps nocturnal BP rise was more closely associated with cardiovascular events than mortality. The patients in this study were much older, and most of them died of infection or other disease, only 11.4% died of cardiovascular events. So it is important to emphasize the importance of controlling BP using ABPM as an indicator to control cardiovascular events⁽¹⁵⁾.

The present study had some limitations. First, as the present study was a cross-sectional study, cause-effect relationship was unclear. Second, in addition to LCI and WMH, cerebral microbleeds is also a form of cerebral small vessel disease, which is reported to be highly prevalent in memory clinic patients and those with Alzheimer's disease^(16, 17). Third, the precise cause of cognitive impairment was not characterized in this study using molecular ligands or pathological confirmation.

Conclusions

The present study showed that nocturnal BP rise was a major risk factor for the development of CI by exacerbation of cerebral microvascular disease. To prevent the progression of CI, management of day-time BP alone is insufficient, and we recommend controlling nocturnal BP rise on the basis of ABPM. CI increased the mortality of the elderly, but the nocturnal BP rise did not. Further studies are required to determine whether lowering nocturnal BP should be targeted to prevent the progression of CI.

Abbreviations

ABPM

ambulatory blood pressure monitoring; MRI:Magnetic Resonance Imaging; CI:cognitive impairment; NCI:non-cognitive impairment group; LCI:lacunar infarcts; WMH:white matter hyperintensities; BP:blood pressure; BPV:blood pressure variation; ABPM:ambulatory blood pressure monitoring; SBP:systolic blood pressure; DBP:diastolic blood pressure; BMI:body mass index; FG:Fasting glucose; HgB:hemoglobin; ALB:albumin; HbA1c:hemoglobin A1c; Cr:creatinine; eGFR:estimated glomerular filtration rate; TC:Total cholesterol; TG:triglycerides; HDL-C:high-density lipoprotein; LDL-C:low-density lipoprotein; ACEI:angiotensin-converting enzyme inhibitor; ARB:angiotensin receptor blocker; CCB:calcium channel blocker; MoCA:Montreal Cognitive Assessment; MMSE:Mini Mental Status Examination ;TIA:transient ischemic attacks.

Declarations

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Ethics approval and consent to participate

The study protocol was approved by the Ethics Committee for Clinical Research of Beijing Friendship Hospital before the performance of the analyses (code: 2018-P2–120-01). This was a retrospective study, and only medical records were analyzed. All procedures involving human participants were performed in accordance with the ethical standards of the Ethics Committee for Clinical Research of Beijing Friendship Hospital and with the Declaration of Helsinki and its later amendments. The need to obtain participants' consent was waived by the ethics committee.

Consent for publication

Not applicable

Availability of data and materials

The datasets used during the current study are available from the corresponding author on reasonable request.

Authors' contributions

Conceived the study protocol and design: XYL and LHW. Collected data: XYL

and WS. Data analysis and interpretation: SY and FF. Statistical analysis: XYL and ZDQ. Drafted the article: XYL. Critically revised the article: XYL, SY, ZDQ, LHW. All authors read and approved the final manuscript.

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Competing interests

The authors declare that they have no competing interests.

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Figures

Figure 1

Flow diagram of the study design.

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Flow diagram of the study design.

Figure 2

Linear regression between nocturnal BP fall and cognitive function. (A) linear regression between nocturnal BP fall and MMSE; (B) linear regression between nocturnal BP fall and MOCA.

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Linear regression between nocturnal BP fall and cognitive function. (A) linear regression between nocturnal BP fall and MMSE; (B) linear regression between nocturnal BP fall and MOCA.

Figure 3

Forest plots of associations between nocturnal BP rise and specific cognitive domains. (A) univariate regression; (B) adjusted for age and gender.

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Forest plots of associations between nocturnal BP rise and specific cognitive domains. (A) univariate regression; (B) adjusted for age and gender.

Figure 4

K-M curves of all-cause mortality. (A) K-M curve of nocturnal BP rise on the all-cause mortality (B) K-M curve of cognitive impairment on the all-cause mortality. Note: NCI, non-cognitive impairment; CI, cognitive impairment.

Figure 4

K-M curves of all-cause mortality. (A) K-M curve of nocturnal BP rise on the all-cause mortality (B) K-M curve of cognitive impairment on the all-cause mortality. Note: NCI, non-cognitive impairment; CI, cognitive impairment.