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ORIGINAL RESEARCH

Association of Longitudinal Change in Ambulatory Blood Pressure With Cognitive Decline in Older Adults

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ABSTRACT

BACKGROUND There has been no study about the association of longitudinal change in ambulatory blood pressure (BP) variability and level with cognitive decline.

OBJECTIVES The purpose of the study was to evaluate whether BP changes via ambulatory BP monitoring predict cognitive decline progression.

METHODS Twice-annual ambulatory BP readings were examined during 5 years and their relationship with changes in the Japanese version of the Montreal Cognitive Assessment (MoCA-J) scores. BP variability was assessed using SD, coefficient of variation, and average real variability (ARV). Cognitive decline, defined as a change in the MoCA-J score, was assessed, with the threshold set at the quartile showing the greatest decrease, which we categorized as cognitive dysfunction (−4 points or less).

RESULTS Among 206 participants (mean age 79.9 [± 7.5] years), baseline 24-hour systolic blood pressure (SBP)/diastolic blood pressure (DBP) averaged 115.2/67.0 mm Hg. Over 4.98 years (IQR: 4.94-5.04 years), MoCA-J scores showed a nonsignificant decline from 20.2 (± 0.4) to 19.9 (± 0.4). A generalized linear mixed model showed that increased SD of daytime SBP (−0.064 [95% CI: −0.121 to −0.007]; $P < 0.029$) and DBP (−0.125 [95% CI: −0.213 to −0.037]; $P = 0.005$) were significantly linked to MoCA-J score decline, with similar trends for most measures except nighttime ARV. Logistic regression revealed higher ORs for cognitive decline with increased SD of daytime SBP (1.52 [95% CI: 1.18-1.96]; $P = 0.001$) and DBP (1.36 [95% CI: 1.09-1.71]; $P = 0.007$), consistent across coefficient of variation and ARV. No association was found between changes in BP level and MoCA-J score decline.

CONCLUSIONS In older adults with controlled BP, increased BP variability was linked to cognitive decline, warranting further study as a prevention target. (JACC Adv. 2025;4:101560) © 2025 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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ABBREVIATIONS AND ACRONYMS

ABPM = ambulatory blood pressure monitoring

ARV = average real variability

BP = blood pressure

CV = coefficient of variation

DBP = diastolic blood pressure

SBP = systolic blood pressure

Cognitive impairment and dementia are global health burdens, and can impede the ability of older individuals to maintain independent lifestyles, ultimately impacting their mortality. Observational studies have linked elevated blood pressure (BP) to heightened risks of lower cognitive performance; the strength of the association peaks during midlife and diminishes in later life.

Several studies have indicated that both high and low BP significantly increase the risk of lower cognitive performance among older adults.[1,2] Although the underlying cause of the observed discrepancy in the impact of low BP on cognitive performance between midlife and late life remains unclear, prior research indicates that, among older adults, in whom cerebral autoregulation is frequently compromised, BP that fluctuates toward lower levels may increase the risk of ischemia, and thereby the risk of impaired cognitive performance.[3,4] This suggests that substantial variability in BP, including instances of declining BP, could further heighten the susceptibility to diminished cognitive performance, as opposed to solely low BP. Indeed, numerous prior studies have documented an association between greater BP variability and decreased cognitive function.[5]

Ambulatory BP monitoring (ABPM) exhibits superior prognostic accuracy compared to office BP measurement.[6,7] Furthermore, beyond merely BP levels, BP variability evaluated through ABPM is an independent predictor of cardiovascular outcomes.[8] Although a number of studies have explored the relationship between BP, as assessed by ABPM, and lower cognitive performance,[9-14] the prevailing emphasis has been on BP status at isolated time points, with scant attention given to longitudinal variations. Additionally, examining this relationship under well-controlled BP conditions is important, as the link between BP variability and event risk is partially influenced by average BP levels.[15]

To address this gap in knowledge, we assessed the association of the longitudinal change in office and ambulatory BP and BP variability assessed by ABPM with subsequent lower cognitive performance in older adults with well-controlled BP.

METHODS

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

This investigation utilized data from the Minamisanriku Study.[16] The Minamisanriku Study is a comprehensive investigation of cardiovascular risk factors in disaster-affected regions, including strategies for the management of such risk factors and ultimately for cardiovascular disease prevention in such areas. Minamisanriku is situated in the northeastern region of Miyagi Prefecture within the Tohoku district of Japan, an area profoundly affected by the Great East Japan Earthquake on March 11, 2011. In response to this disaster, we implemented an information and communication technology-based home BP monitoring system to mitigate cardiovascular risks associated with the catastrophe.[17] Following confirmation of stable home BP levels, regular ABPM sessions were initiated twice a year in summer (July to September) and winter (December to March of the following year) for outpatients at Minamisanriku Hospital, which is located within the disaster zone, starting from the winter of 2012. The Japanese version of the Montreal Cognitive Assessment (MoCA-J) was administered to consenting patients between July and September in 2016 and between July and September in 2021. For the purposes of this study, we selected patients who underwent both MoCA-J assessments and ABPM sessions in both 2016 and 2021. In 2016, 322 individuals underwent both ABPM and MoCA-J. We excluded participants who died (n = 44), as well as those who moved away from the study region (n = 8), those who could not perform ABPM due to a disability (n = 44), and those who refused ABPM (n = 17). Among the remaining 209 participants, 3 participants had an average of fewer than 3 nighttime BP readings. The final study sample was thus composed of 206 individuals (**Figure 1**).

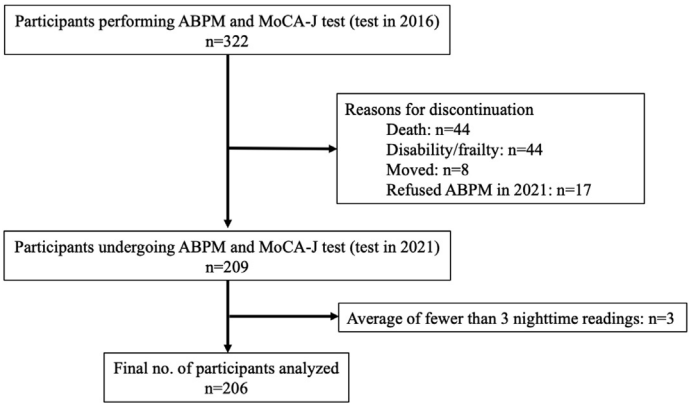
BP MEASUREMENTS. Data from ABPM performed twice a year from the summer of 2016 to the summer of 2021 (a total of 11 times) were utilized in this study. ABPM was performed with a validated automatic device (TM-2431/2433, A&D Co) that recorded BP using an oscillometric method at 30-minute intervals throughout the 24-hour day. Nighttime BP was defined as the average BP over the period from when patients went to bed until they woke in the morning. Daytime BP was defined as the average BP for the rest of the day. For each individual, we determined the SD, the coefficient of variation (CV), and the average real variability (ARV) for systolic blood pressure (SBP) and diastolic blood pressure (DBP) in daytime and nighttime. These indexes of BP variability assessed by ABPM have been used in other studies.[18] For analysis,

ambulatory BP recordings had to include at least 6 daytime and 3 nighttime readings.[19] The data used for the quality control of ABPM are shown in Supplemental Table 1. Office BP was measured at each visit using a validated cuff oscillometric device according to the Japanese Society of Hypertension guidelines.[20] Two consecutive BP measurements were taken at a 1 minute interval, and the average of the measurements was used as the office BP value. Given that the twice-annual ABPMs consistently followed outpatient visits, the office BP readings obtained prior to the ABPM were utilized for this analysis.

COGNITIVE ASSESSMENT. We used the MoCA-J as a cognitive screening tool. The diagnostic accuracy of MoCA-J has been reported to be almost the same as that of the original version of MoCA for both mild cognitive impairment and Alzheimer disease.[21] MoCA-J scores range from 0 to 30. Given the absence of firmly established criteria delineating a clinically significant decline in the comprehensive MoCA-J score, we adopted an operational definition approach as follows. Initially, we computed the variance between each participant's baseline and subsequent assessments. Next, we analyzed the distribution of these individual scores and determined, for each cognitive outcome, the threshold corresponding to the quartile representing the greatest decrease in the MoCA-J score, which we defined as cognitive dysfunction (−4 points or less in this study).[22]

STATISTICAL ANALYSIS. The baseline characteristics of the study participants were reported as mean ± SD (for continuous variables) or counts and percentages (for categorical variables). The office BP and ABPM variables at baseline were categorized into tertiles. Differences in the change in MoCA-J score from baseline to follow-up among the tertiles of each BP variable at baseline were assessed using analysis of covariance models. Analysis of covariance models were adjusted for age, traditional cardiovascular risk factors (male, body mass index, smoking, dyslipidemia, and diabetes), prevalent cardiovascular events, use of antihypertensive medication, and MoCA-J score at baseline, and the results are presented as the estimated means and 95% CIs. Changes in BP level and variability over time were assessed using repeated measures mixed-effect models using the available BP data at each time point without imputation for missing values. We used a generalized linear mixed model for the association between BP indexes over time and the change in MoCA-J score adjusted for age, traditional cardiovascular risk factors, prevalent cardiovascular events, use of antihypertensive medication, and MoCA-J score at baseline. For the association between BP indexes over time and the lowest quartile of change in the MoCA-J score as a binary outcome, we used a generalized logistic regression mixed model adjusted for the same covariates. Two-sided values of $P < 0.05$ were defined as statistically significant. All statistical analyses were performed with Stata ver. 15.0 software (StataCorp).

FIGURE 1 Participant Selection



ABPM = ambulatory blood pressure; MoCA-J = the Japanese version of the Montreal Cognitive Assessment.

RESULTS

Supplemental Table 2 showed the comparison of baseline characteristics of participants who were included in the current study and those who were not included. At study entry, the mean age among the 206 participants was 79.8 ± 7.5 years, and 31.1% (65/206) were male. A total of 190 participants (92.2%) were taking antihypertensive drugs and the mean of 24-hour BP levels was 115.2 ± 9.4/67.0[5,8] mm Hg. The prevalences of controlled office BP (<140/90 mm Hg), 24-hour BP (<135/85 mm Hg), daytime BP (<135/85 mm Hg), and nighttime BP (<120/70 mm Hg) were 58.3% (86/206), 92.7% (191/206), 92.2% (190/206), and 84.0% (173/206), respectively. The mean MoCA-J score was 20.2 ± 0.4. The summary characteristics of the participants at baseline are presented in **Table 1**.

After a follow-up duration of approximately 5 years (mean 4.98 years [IQR: 4.94-5.04 years]), a decrease in MoCA-J scores was observed from a mean of 20.2 ± 0.4 to 19.9 ± 0.4, although the difference was not statistically significant. **Figure 2A** shows the office,

TABLE 1 Baseline Characteristics (N = 206)

Age, y	79.9 ± 7.5
Male, %	65 (31.6)
Body mass index, kg/m^2	25.6 ± 3.7
Current smoker, %	8 (3.9)
Alcohol, %	48 (23.3)
Diabetes, %	65 (31.6)
Dyslipidemia, %	141 (68.5)
Prevalent cardiovascular disease, %	9 (4.4)
Atrial fibrillation, %	10 (4.9)
Antihypertensive drug	
Calcium channel blocker, %	175 (85.0)
Angiotensin-converting enzyme inhibitor, %	4 (1.9)
Angiotensin II receptor blocker, %	172 (83.5)
Diuretics, %	90 (43.7)
Alpha blocker, %	9 (4.4)
Beta-blocker, %	16 (7.8)
Antiplatelet drug, %	9 (4.4)
Office SBP, mm Hg	135.0 ± 16.7
Office DBP, mm Hg	73.7 ± 9.8
24-hour SBP, mm Hg	115.2 ± 9.4
24-hour DBP, mm Hg	67.0 ± 5.8
Daytime SBP, mm Hg	119.2 ± 10.5
Daytime DBP, mm Hg	69.7 ± 6.6
Nighttime SBP, mm Hg	107.1 ± 10.7
Nighttime DBP, mm Hg	61.7 ± 6.0
SD of daytime SBP, mm Hg	18.2 ± 6.0
SD of daytime DBP, mm Hg	11.3 ± 3.6
SD of nighttime SBP, mm Hg	12.0 ± 4.1
SD of nighttime DBP, mm Hg	8.1 ± 2.9
CV of daytime SBP, %	15.2 ± 4.8
CV of daytime DBP, %	16.3 ± 5.4
CV of nighttime SBP, %	11.2 ± 3.8
CV of nighttime DBP, %	13.1 ± 4.6
ARV of daytime SBP, mm Hg	15.5 ± 5.5
ARV of daytime DBP, mm Hg	9.9 ± 3.5
ARV of nighttime SBP, mm Hg	10.8 ± 3.5
ARV of nighttime DBP, mm Hg	7.3 ± 2.6
MoCA-J score	20.2 ± 0.4

Values are mean ± SD or n (%).

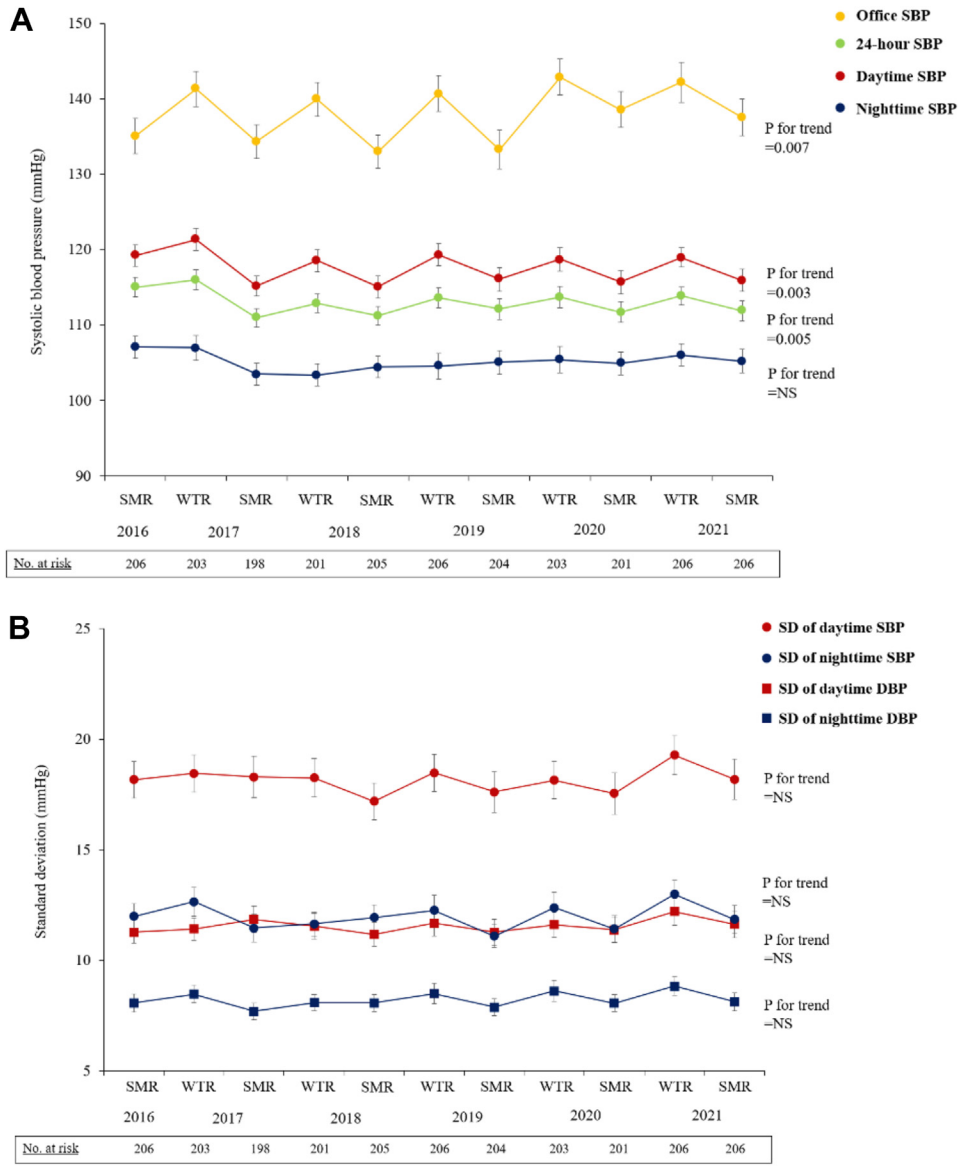
ARV = average real variability; CV = coefficient of variation; DBP = diastolic pressure; MoCA-J = Japanese version of the Montreal Cognitive Assessment; SBP = systolic blood pressure.

24 hours, daytime, and nighttime SBP values calculated at each visit from baseline to the last visit. Office SBP (estimate 0.6 [95% CI: 0.2-1.9] mm Hg, $P = 0.007$) gradually increased over the follow-up period, while 24-hour SBP (−0.3 [95% CI: −0.6 to −0.1] mm Hg, $P = 0.005$) and daytime SBP (−0.4 [95% CI: −0.7 to −0.1] mm Hg, $P = 0.003$) gradually decreased over the follow-up, and no nighttime SBP changes were observed (−0.1 [95% CI: −0.3 to −0.2] mm Hg, $P = 0.604$). No changes in any DBP parameters were observed over the follow-up period (Supplemental Figure 1). In regard to the parameters of BP variability, no changes were observed in any of the SBP and DBP variability parameters during the follow-up period (**Figure 2B**, Supplemental Figures 2 and 3).

BASELINE BLOOD PRESSURE/VARIABILITY AND CHANGE IN THE MoCA-J SCORE. When participants were stratified according to BP levels at baseline, those in the lowest tertile of 24-hour SBP showed a significant cognitive decline (mean: −1.0 [95% CI: −1.9 to −0.2]). This trend was observed in the lowest tertile of daytime SBP (mean: −1.4 [95% CI: −2.3 to −0.5]). We observed no association between cognitive change over time and office SBP and DBP and other ABPM variables. When participants were stratified according to BP variability at baseline, those in the highest tertile of the SD (mean: −1.2 [95% CI: −2.1 to −0.3]) and CV (mean: −1.1 [95% CI: −2.0 to −0.2]) of daytime DBP showed a significant cognitive decline. This trend was marginally observed in the highest tertile of the CV of daytime SBP and DBP and CV of nighttime SBP. We observed no association between cognitive change over time and other BP variability parameters (Supplemental Table 3).

LONGITUDINAL CHANGE IN BLOOD PRESSURE VARIABILITY/LEVEL AND MoCA-J SCORE DECLINE. Mixed model linear regression analysis with adjustment revealed that increased changes in the SD of daytime SBP (estimate: −0.064 [95% CI: −0.121 to −0.007]; $P = 0.029$) and DBP (estimate: −0.125 [95% CI: −0.213 to −0.037]; $P = 0.005$) were significantly associated with MoCA-J score decline. A similar trend for association was found for the SD of nighttime SBP (estimate: −0.097 [95% CI: −0.177 to −0.016]; $P = 0.019$) and DBP (estimate: −0.212 [95% CI: −0.330 to −0.094]; $P < 0.001$). Moreover, increased changes in the CV of daytime SBP (estimate: −0.095 [95% CI: −0.164 to −0.025]; $P = 0.008$) and DBP (estimate: −0.088 [95% CI: −0.150 to −0.026]; $P = 0.006$) and nighttime SBP (estimate: −0.104 [95% CI: −0.194 to −0.014]; $P = 0.023$) and DBP (estimate: −0.116 [95% CI: −0.191 to −0.042]; $P = 0.002$) were significantly associated with MoCA-J score decline. Similar results were found for the ARV of daytime SBP (estimate: −0.070 [95% CI: −0.130 to −0.009]; $P = 0.024$) and DBP (estimate: −0.120 [95% CI: −0.210 to −0.031]; $P = 0.008$). Although there was a marginal association between increased ARV of nighttime DBP and MoCA-J score decline, we observed no association between ARV of nighttime SBP and MoCA-J score decline. Conversely, there was no association between longitudinal change in BP level, including office, 24 hours, daytime and nighttime SBP and DBP, and MoCA-J score decline (**Table 2**).

FIGURE 2 Mean Office and Ambulatory Systolic Blood Pressure and Daytime and Nighttime Blood Pressure Variability Over Time



Mean office and ambulatory systolic blood pressure (A) and daytime and nighttime blood pressure variability (B) over time shown are means with 95% CI. DBP = diastolic blood pressure; SBP = systolic blood pressure; SMR = summer; WTR = winter.

Binary logistic regression analysis with adjustment demonstrated that increased SDs of daytime SBP (OR per 1 SD: 1.52 [95% CI: 1.18-1.96]; $P = 0.001$) and DBP (OR per 1 SD: 1.36 [95% CI: 1.09-1.71]; $P = 0.007$) had significant ORs for cognitive decline (−4 points or less). Similar results were found for the CVs of daytime SBP (OR per 1 SD: 1.54 [95% CI: 1.20-1.97]; $P = 0.001$) and DBP (OR per 1 SD: 1.37 [95% CI: 1.07-1.77]; $P = 0.014$) and ARVs of daytime SBP (OR per 1 SD: 1.49 [95% CI: 1.15-1.93]; $P = 0.003$) and DBP (OR per 1 SD: 1.50 [95% CI: 1.15-1.96]; $P = 0.003$). We observed no association between serial change in nighttime BP variability represented as the SD, CV, or ARV and cognitive decline. Moreover, there was no association between longitudinal change in BP levels, including office, 24 hours, daytime and nighttime SBP and DBP, and cognitive decline (Table 3).

TABLE 2 Results of Generalized Linear Mixed Model Analysis Conducted to Assess the Longitudinal Associations of BP Parameters Over Time With Change in MoCA-J Score

	Estimate (95% CI)	*P* Value
Office SBP	−0.009 (−0.030 to 0.011)	0.360
Office DBP	−0.008 (−0.042 to 0.027)	0.667
24-hour SBP	0.009 (−0.027 to 0.044)	0.630
24-hour DBP	−0.013 (−0.076 to 0.049)	0.677
Daytime SBP	0.015 (−0.017 to 0.047)	0.369
Daytime DBP	0.001 (−0.054 to 0.056)	0.967
Nighttime SBP	−0.009 (−0.041 to 0.022)	0.558
Nighttime DBP	−0.039 (−0.095 to 0.018)	0.183
SD of daytime SBP	−0.064 (−0.121 to −0.007)	0.029
SD of daytime DBP	−0.125 (−0.213 to −0.037)	0.005
SD of nighttime SBP	−0.097 (−0.177 to −0.016)	0.019
SD of nighttime DBP	−0.212 (−0.330 to −0.094)	<0.001
CV of daytime SBP	−0.095 (−0.164 to −0.025)	0.008
CV of daytime DBP	−0.088 (−0.150 to −0.026)	0.006
CV of nighttime SBP	−0.104 (−0.194 to −0.014)	0.023
CV of nighttime DBP	−0.116 (−0.191 to −0.042)	0.002
ARV of daytime SBP	−0.070 (−0.130 to −0.009)	0.024
ARV of daytime DBP	−0.120 (−0.210 to −0.031)	0.008
ARV of nighttime SBP	−0.038 (−0.128 to 0.051)	0.400
ARV of nighttime DBP	−0.124 (−0.254 to 0.007)	0.063

Each model was adjusted by age, sex, body mass index, smoking, diabetes, dyslipidemia, prevalent cardiovascular disease, use of antihypertensive medication, and MoCA-J score at the baseline.

Abbreviations as in Table 1.

DISCUSSION

In the present analysis conducted in older adults with good ambulatory BP control, increased BP variability was associated with subsequent cognitive decline after a 5-year follow-up independent of conventional cardiovascular risk factors, antihypertensive medication use, and baseline cognitive level. A similar trend for association was observed for BP variability assessed at baseline. Conversely, with respect to the association between average BP level and cognitive decline, longitudinal change in ambulatory BP level was not associated with subsequent cognitive decline, but lower ambulatory BP level at baseline tended to be associated with a risk for subsequent cognitive decline. Neither office BP at baseline nor office BP changes were associated with a risk of subsequent cognitive decline (**Central Illustration**).

Increased BP variability assessed by ABPM has been reported to be associated with target organ damage and cardiovascular outcome.[8] Although several studies have also reported an association between ABPM-assessed BP variability and cognitive function, those studies had notable limitations.[9-14] Namely, some of them were based on a cross-sectional analysis,[11-14] while others focused on the association between BP variability at baseline and cognitive change.[9,10] To the best of our knowledge, this is the first study about the risk of longitudinal BP variability with cognitive decline in older adults. Although the mechanism underlying the association between BP variability and cognitive decline is unclear, increased BP variability might accelerate arterial stiffness and vice versa. Sudden decreases in BP related to BP variability might reduce perfusion of the cerebral white matter,[23] while sudden increases in BP might injure the small cerebral arteries, which are exposed to a high level of pressure without attenuation from the large artery, especially in older adults prone to arterial stiffness, because increased arterial stiffness is not available to attenuate the pulse transmitted to the peripheral arteries.[24]

In this study, the trend for the association between nighttime BP variability and cognitive deterioration was weaker than that for daytime BP variability. The reasons for this are unclear. A previous study that investigated the association between BP variability assessed by ABPM at baseline and the decline of cognitive function over a 5-year follow-up period showed that daytime BP variability was associated with cognitive decline, while nighttime BP variability was not.[9] Another study demonstrated that daytime BP variability assessed by ABPM at baseline was associated with the progression of cerebral small vessel disease based on magnetic resonance imaging after 4.4 years of follow-up.[25] BP variability is a complex phenomenon produced by multiple factors. BP response to physical activity is one of the determinant physiological factors of BP variability. Older adults typically exhibit lower levels of physical activity compared to younger individuals. Consequently, an increase in daytime BP variability beyond that attributable to the activity level may indicate underlying pathophysiological factors that could contribute to cognitive deterioration.

This study demonstrated an association between lower ambulatory BP levels at baseline and cognitive decline; however, there were no longitudinal BP levels showing statistical significance. Although an earlier study reported that low daytime SBP assessed by ABPM (≤128 mm Hg) at baseline was associated with a risk of cognitive decline as evaluated by the Mini-Mental State Examination score after a median follow-up duration of 9 months in 172 patients with an average age of 70 years,[26] that study did not assess longitudinal ambulatory BP measures. Another cross-sectional study similarly reported that lower BP levels were associated with cognitive impairment.[13] The

TABLE 3 Results of Generalized Logistic Regression Mixed Model Analysis Conducted to Assess the Longitudinal Associations of BP Parameters Over Time (Per 1SD) With the Lowest Quartile of Reduction (−4 Points or Less) in MoCA-J Score

	OR (95% CI)	*P* Value
Office SBP	0.97 (0.75-1.27)	0.848
Office DBP	1.26 (0.97-1.63)	0.083
24-hour SBP	1.04 (0.81-1.33)	0.743
24-hour DBP	0.92 (0.63-1.36)	0.677
Daytime SBP	1.01 (0.79-1.30)	0.926
Daytime DBP	1.11 (0.87-1.41)	0.393
Nighttime SBP	1.11 (0.86-1.43)	0.417
Nighttime DBP	1.19 (0.94-1.50)	0.146
SD of daytime SBP	1.52 (1.18-1.96)	0.001
SD of daytime DBP	1.36 (1.09-1.71)	0.007
SD of nighttime SBP	1.20 (0.93-1.54)	0.152
SD of nighttime DBP	1.18 (0.95-1.47)	0.127
CV of daytime SBP	1.54 (1.20-1.97)	0.001
CV of daytime DBP	1.37 (1.07-1.77)	0.014
CV of nighttime SBP	1.17 (0.91-1.51)	0.212
CV of nighttime DBP	1.14 (0.89-1.46)	0.305
ARV of daytime SBP	1.49 (1.15-1.93)	0.003
ARV of daytime DBP	1.50 (1.15-1.96)	0.003
ARV of nighttime SBP	0.94 (0.72-1.23)	0.659
ARV of nighttime DBP	1.09 (0.84-1.41)	0.516

One SD increment of each BP parameter is as follows: office SBP, per 17.5 mm Hg; office DBP, per 10.4 mm Hg; 24-hour SBP, 9.6 mm Hg; 24-hour DBP, 6.2 mm Hg; daytime SBP, 10.7 mm Hg; daytime DBP, 6.9 mm Hg; nighttime SBP, 11.2 mm Hg; nighttime DBP, 6.6 mm Hg; SD of daytime SBP, 6.3 mm Hg; SD of daytime DBP, 4.1 mm Hg; SD of nighttime SBP, 4.4 mm Hg; SD of nighttime DBP, 3.0 mm Hg; CV of daytime SBP, 5.1%; CV of daytime DBP, 5.9%; CV of nighttime SBP, 4.0%; CV of nighttime DBP, 4.9%; ARV of daytime SBP, 6.2 mm Hg; ARV of daytime DBP, 4.3 mm Hg; ARV of nighttime SBP, 3.9 mm Hg; ARV of nighttime DBP, 2.8 mm Hg. Each model was adjusted by age, sex, body mass index, smoking, diabetes, dyslipidemia, prevalent cardiovascular disease, use of antihypertensive medication, and MoCA-J score at the baseline.

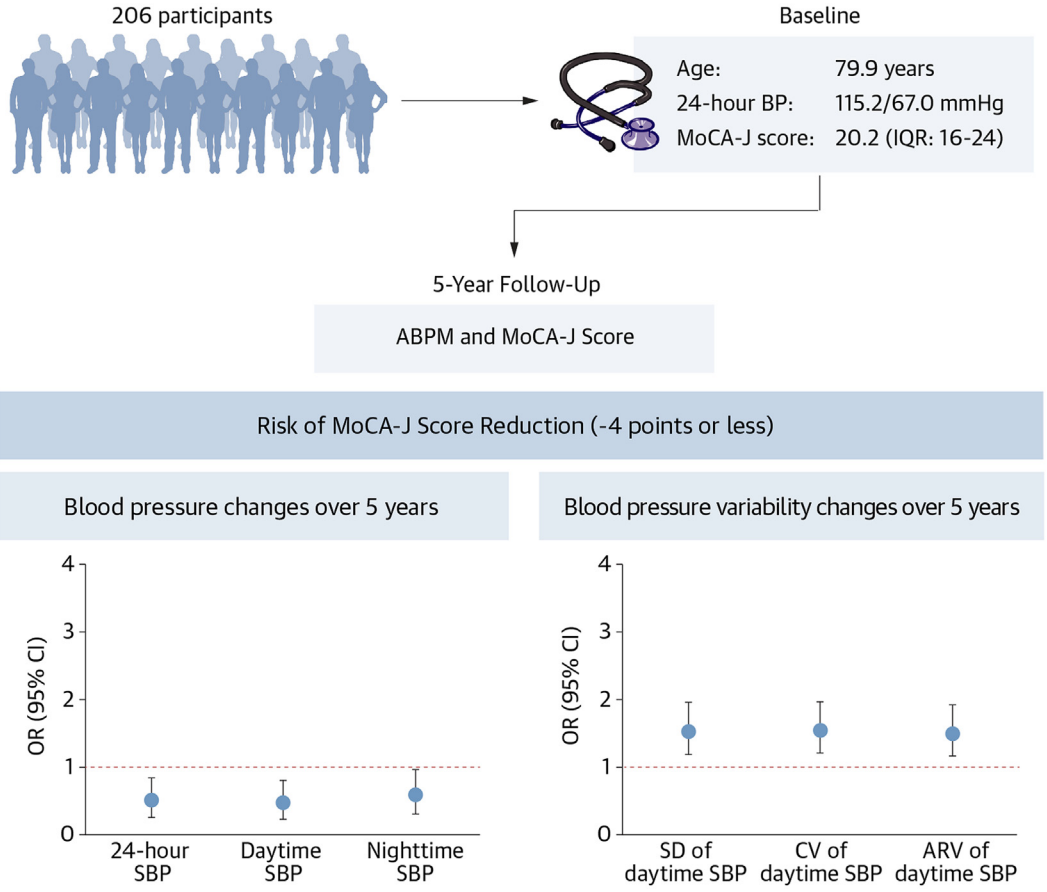
Abbreviations as in Table 1.

reason that only lower baseline BP measures or BP measures at a single time point, not longitudinal BP measures, were associated with cognitive decline might be explained by reverse causality. For example, cognitive dysfunction will lead individuals to reduce their physical activity, which in turn will lower their daytime BP, because activity is the most important determinant factor of BP. Serial tracking data could help uncover reverse causality or else attenuate its influence in data analysis. Moreover, measuring BP multiple times over several years also decreases the chance of bias caused by differences between individuals.[27] In older adults, impaired autoregulation of cerebral blood flow related to aging may easily lead to a decrease in BP, and reduced cerebral blood flow could contribute to cerebral hypoperfusion, which is further linked to neurodegenerative alterations.[28] Nonetheless, our findings provide a more accurate picture of the relation between longitudinal high-BP variability exposure and cognitive impairment and clearly indicate that there is no harm in lower BP levels in terms of the progression of cognitive decline in older adults with good 24-hour BP control. Furthermore, well-managed BP may have weakened the association between BP variability and cognitive decline, given that the risk associated with BP variability is partially affected by average BP levels.[15]

In this study, neither office BP at baseline nor longitudinal office BP was associated with cognitive decline. In a recent meta-analysis of studies sharing a common population-based cohort, there was a lack of agreement in regard to the association between elevated office BP and risk of dementia or cognitive decline. Even among intervention studies for office BP, the conclusions regarding such an association are inconsistent. The SPRINT MIND (Systolic Blood Pressure Intervention Trial-Memory and Cognition IN Decreased Hypertension trial examining the effectiveness of different BP targets in patients at high risk for hypertension aged ≥50 years has shown that intensive treatment targeting an SBP <120 mm Hg had a lower risk of mild cognitive impairment and dementia outcomes compared to a standard treatment targeting SBP <140 mm Hg,[29] while in the HOPE-3 (Heart Outcomes Prevention Evaluation-3) trial the intervention of antihypertensive treatment did not affect cognitive decline in low-risk older people.[30] This may underscore the limitation of office BP for assessing the risk of cognitive deterioration or dementia.

Some limitations of the present study should also be acknowledged. First, the data analyzed in this study were limited to a single institution where ABPM was regularly conducted. Institutions that implement and manage ABPM with a similar frequency might be scarce, making this population a limited group. Moreover, the analysis of this study was performed in individuals who provided consent to undergo ABPM measurements and a cognitive test. Candidates who refused ABPM or the cognitive test were excluded, making the presence of selection bias likely. Furthermore, individuals with disabilities or frailty were excluded from this study. Therefore, the findings may primarily apply to the healthiest subset of the older population. Secondly, owing to the nature of retrospective studies, the influence of unmeasured confounding factors on our results cannot be eliminated, thereby hindering further steps toward conclusively defining causal

CENTRAL ILLUSTRATION **Longitudinal Change in Ambulatory Blood Pressure Level and Variability With Cognitive Decline for 206 Subjects**



Hoshide S, et al. JACC Adv. 2025;4(2):101560.

Longitudinal change in ambulatory blood pressure level and variability with cognitive decline for 206 subjects (left); longitudinal associations of ambulatory blood pressure levels (per 1 SD) with the lowest quartile of reduction (-4 points or less) in MoCA-J score (right); longitudinal associations of ambulatory blood pressure variability (per 1 SD) with the lowest quartile of reduction (-4 points or less) in MoCA-J score. Abbreviations as in Figures 1 and 2.

relationships. In this study, there was no significant change in the MoCA-J score from baseline to follow-up, with most participants scoring below the 26-point threshold. Previous studies have reported a significant correlation between reductions in regional cerebral blood flow and MoCA-J scores, even among individuals with scores below the abnormal threshold.[31] Thus, our findings suggest that even slight changes in MoCA-J scores may hold clinical significance in this population. Finally, this study employed complete-case analysis due to the presence of missing data. While a detailed analysis of missing data patterns is presented in Supplemental Materials, some degree of bias due to data exclusion cannot be entirely ruled out.

CONCLUSIONS

Based on our observation, in older adults with good control of ambulatory BP, longitudinal increases in ambulatory BP variability were associated with subsequent cognitive decline. Further studies are required to elucidate the mechanism underlying the association between BP variability and cognitive impairment and the potential of BP variability as a target for the prevention of cognitive decline.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Our findings reinforce the evidence from previous limited studies on BP variability and levels at isolated time points and cognitive decline by examining changes in longitudinal BP variability and levels.

TRANSLATIONAL OUTLOOK: Further research is needed to clarify the mechanisms linking BP variability with cognitive impairment and to explore the potential of targeting BP variability for preventing cognitive decline.

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APPENDIX For supplemental methods, tables, and figures, please see the online version of this paper.