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Relationships between 24-Hour Blood Pressures, Subcortical Ischemic Lesions, and Cognitive Impairment

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Background and Purpose The most important treatment for subcortical vascular dementia (SVaD) is controlling the blood pressure (BP). However, the few studies that have investigated the relationships between diurnal BP rhythm and subcortical ischemic vascular cognitive impairment have produced inconclusive results. In the study presented here, the 24-hour BP values of three groups of subjects-patients with subcortical vascular mild cognitive impairment (SvMCI), patients with SVaD, and normal controls-were compared using working criteria and 24-hour ambulatory BP (ABP) monitoring.

Methods The subjects (42 patients with SVaD, 37 patients with SvMCI, and 30 controls) were selected according to the study's inclusion/exclusion criteria. All subjects underwent brain magnetic resonance (MR) imaging and MR angiography, detailed neuropsychological testing, and 24-hour ABP monitoring.

Results The prevalence of nondippers differed markedly between the control group and both the SVaD and SvMCI groups. Loss of nocturnal dipping was significantly associated with SVaD [odds ratio (OR), 4.827; 95% confidence interval (CI), 1.07-12.05].

Conclusions It was found that SVaD is associated with loss of nocturnal BP dipping combined with increased pulse pressure and systolic BP (SBP) variability. Correction of these factors could therefore be important in the prevention of SVaD, independent of measures used to reduce BP.
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Key Words 24-hour blood pressure values, subcortical vascular mild cognitive impairment, subcortical vascular dementia.

Introduction

Small-vessel disease in the brain accounts for one quarter of ischemic strokes and is probably the main cause of vascular cognitive impairment.[1,2] Small-vessel disease manifests as abnormalities on magnetic resonance (MR) imaging (MRI), mainly in subcortical areas such as the basal ganglia, frontal white matter, periventricular white matter, and the bilateral thalamic areas. Although there are no consensus criteria for it, subcortical vascular dementia (SVaD) is thought to be the natural successor to subcortical vascular mild cognitive impairment (SvMCI), in the same way that vascular dementia is the successor to vascular mild cognitive impairment (MCI).[2]

After age, hypertension is the most important risk factor for small-vessel disease, and it is becoming increasingly clear that there is a complex and dynamic relationship between blood pressure (BP) and subcortical white-matter ischemic injury. It has been found that an elevated BP in midlife is associated with a higher prevalence of white-matter injury in the brain and cognitive decline in subsequent years, and that a lower BP in old age is associated with worse intellectual function.[3-7] However, no clear relationship has been demonstrated between diurnal BP rhythm and subcortical ischemic vascular cognitive impairment (VCI).

Noninvasive ambulatory BP (ABP) monitoring is used to study BP under normal living conditions as it provides a reliable estimate of the habitual diurnal BP rhythm, which

may be used to independently predict hypertension-related complications.[8] In normal subjects, the mean nocturnal systolic BP (SBP) is 10-20% lower than the mean daytime SBP, a phenomenon known as dipping.[9] Alteration of this nocturnal dip in BP, either nondipping (where the nocturnal SBP decrease is less than 10% of the daytime SBP) or hyperdipping (where the nocturnal SBP decrease is more than 20% of the daytime SBP), is associated with an elevated risk of end-organ injury, particularly to the heart, brain, and kidneys.[8,10-12] Many studies have shown that the degree of nocturnal BP dipping determines the consequent type of cerebrovascular injury. O'Brien et al.[10] reported that strokes are significantly more likely to occur in nondipping hypertensive persons than in dipping hypertensive ones. More recently, Staessen et al.[11] found that the incidences of stroke and myocardial infarction were higher in nondippers than in those with a normal dipping pattern. However, the few studies that have been published on the relationship between the ABP profile and the progression of small-vessel disease in the brain have produced conflicting results. Some studies suggest that the severities of small-vessel disease and cognitive dysfunction are affected by the loss of nocturnal BP dipping or SBP variability, whereas others have produced opposing results. This apparent disparity may be due to differences in the number of study subjects and the methodologies and assessment techniques applied in the different studies.[13,14]

SvMCI, which is the preclinical stage of SVaD, has become far more important than SVaD itself due to the progression of small-vessel disease, although no definite criteria have been established. This recent recognition and the lack of criteria are due to there being few published data related to SvMCI. However, much of the established knowledge on SvMCI, which has been accrued using modified MCI criteria, indicates that white-matter lesions (WMLs) revealed by MRI and the clinical vascular symptoms or signs facilitate the diagnosis of SvMCI.

The study presented here analyzed and compared 24-hour BP values of control subjects and SvMCI and SVaD patients, with the aim of determining whether 24-hour BP patterns differ between SvMCI and SVaD patients.

Methods

Subject selection

SvMCI and SVaD patients were selected consecutively from the memory disorder clinics at Ewha Womans University Hospital, Seoul National University Bundang Hospital, and Konyang University Hospital, South Korea, and normal controls were recruited at the Department of Cardiology, between March 2006 and April 2008. All of the subjects gave their informed consent to participate in the study and underwent brain MRI and MR angiography. The impairments in each of the cognitive domains were evaluated with the aid of a detailed neuropsychological test, the Instrumental Activities of Daily Living (I-ADL) scale, and the overall severity was assessed using the Clinical Dementia Rating (CDR) scale.

The subjects were assigned to one of the three groups according to the following inclusion criteria:

1) Control group: Subjects in this group exhibited cognitivefunction performances in the neuropsychological tests that were within the normal range, and had no lobar or cortical lesions on MRI.

2) SVaD/SvMCI groups: The etiology underlying the cognitive impairment of the SVaD and SvMCI patients was most probably the WMLs on MRI with no evidence of any other etiology, such as prominent hippocampal atrophy, cortical or large territorial infarction, or severe amnesia of the encoding deficit type.

3) SVaD group: These patients met the criteria for vascular dementia described by the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition, the objective cognitive decline below the 16th percentile of norms on standardized neuropsychological tests, and they had CDR, I-ADL, and Hachinski ischemic (HI) scores of $\geq$1, $\geq$8, $\geq$5, respectively. We excluded those SVaD patients with a CDR score of 0.5 and an I-ADL score of 8 (i.e., very mild stage of the disease).

4) SvMCI group: The objective cognitive decline of these patients was below the 16th percentile of norms on standardized neuropsychological testing, and they exhibited CDR, I-ADL, and HI scores of 0.5, <8, and $\geq$5, respectively.[15,16]

Conventional risk factors

Hypertension was diagnosed if the patient had either previously used or was currently using antihypertensive agents at the time of the hospital visit, and if the patient had a mean SBP of $\geq$140 mmHg or a mean diastolic BP (DBP) of $\geq$90 mmHg, as measured on at least two separate occasions with the patient in a sitting position. Diabetes mellitus was defined as either a fasting glucose level of >126 mg/dL (as measured on more than two occasions) or if the patient was currently using antidiabetic medication at the time of their hospital visit. The presence of dyslipidemia was indicated by a fasting total cholesterol level of >220 mg/dL, a fasting triglyceride level of >200 mg/dL, or the use of a lipidlowering agent at the time of the patient's hospital visit. Cigarette smoking was defined as being a current smoker at the time of the patient's hospital visit. None of the patients had a history of cardiovascular or cerebrovascular disease.

Blood pressure measurement

Noninvasive ABP monitoring was performed on weekdays, starting early in the morning. Measurements were taken from the nondominant arm every hour during the day and night. The subjects were instructed to perform their normal daily activities and to adhere to their normal sleep patterns. For analysis, the daytime and nighttime episodes were defined as those occurring between 07 : 00 and 21 : 00 hours and between 22 : 00 and 06 : 00 hours, respectively. The subjects' mean BP, mean heart rate, and diurnal BP rhythm were determined for these episodes. The mean SBP, DBP, mean arterial pressure, pulse pressure (PP), and heart rate values were computed for the daytime, nighttime, and 24-hour episodes using a custom-made computer program running on a portable autonomic function recorder.

According to recently issued guidelines,[1,16,17] our participants could be classified according to their BP characteristics and dipper status. The ABP values were dichotomized into low and high groups as follows: daytime SBP (≤135 and >135 mmHg, respectively), daytime DBP (≤80 and >80 mmHg, respectively), nighttime SBP (≤120 and >120 mmHg, respectively), and nighttime DBP (≤70 and >70 mmHg, respectively). The patients were also divided into three dipper-status categories for nocturnal BP: dippers, non-dippers, and reverse dippers, defined as a difference in the mean BP between the daytime and nighttime hours of >10%, 0-10%, and <0, respectively. SBP variability and PP could be divided into two categories: low (≤15 mmHg) and high (>15 mmHg) SBP variability, and low (≤50 mmHg) and high (>50 mmHg) PP.

MRI investigation and white-matter lesions scoring

MRI scans were obtained using a 3.0-T device (Intera NT, Philips, Eindhoven, the Netherlands) and a 1.5-T device (Avanto Syngo, Siemens, Erlargen, Germany). The scan protocol included determining the axial proton density, T2-weighted axial imaging, fluid-attenuated inversion recovery (FLAIR) sequences, T1-weighted axial imaging, and MR angiography at a slice thickness of 5 mm. Lacunes were defined as lesions that were 3-15 mm in diameter and that exhibited a low-intensity signal on the T1-weighted images, but a high-intensity signal on the T2-weighted and FLAIR images. WMLs were defined as diffuse hyperintensities located in the subcortical and periventricular white matter on T2-weighted images. For MRI, the number of lacunes was graded as follows: absent, 0; one or two lacunes, 1; three to five lacunes, 2; and more than five lacunes, 3. A WML was regarded as a periventricular hyperintensity (PVH) when it was adjacent to a ventricle; otherwise, the lesion was deemed to be a deep white-matter hyperintensity (DWH). The PVHs and DWHs were scored semiquantitatively according to the classification of Fazekas.[17] The PVHs were classified as follows: absent, 0; cap or pencil-thin lining, 1; smooth halo, 2; and irregular PVH extending into the deep white matter, 3. The DWHs were classified as follows: absent, 0; punctuated, 1; becoming confluent, 2; and confluent, 3. The MRI data were evaluated by two neurologists who were blinded to both the BP data and the clinical findings.

Cognitive assessment

Cognitive function was tested by applying the Seoul Neuropsychological Screening Battery, which is a standardized neuropsychological battery that comprises tests for attention, visuospatial function, verbal and visual memory functions, language-related function, and frontal executive functions.[18] These tests include the digit span test (forward and backward) for attention, the Korean version of the Boston Naming Test, written calculations for testing language and related functions, Rey-Osterrieth Complex Figure Test (RCFT) copying, time and place orientation, free recall, delayed recall trials and recognition scores of the Seoul Verbal Learning Test and RCFT immediate, 20-min-delayed recall trials, and recognition scores for memory. The following tests were also applied to assess frontal executive function: impersistence, contrasting program, go/no-go test, fist-edge-palm test, Luria loop, phonemic and semantic Controlled Oral Word Association Test, and Stroop Test.

Statistical analysis

The demographics, risk factors, and BP data of the study groups were compared first. The continuous variables are expressed as mean±SD values, and the categorical variables are expressed as the percentage of patients affected. The clinical variables in the three study groups were compared, with the BP data analyzed using one-way ANOVA and through multiple comparisons of the three groups employing Tukey testing. The associations were evaluated by estimating the odds ratios (ORs) for SVaD and its risk factors, as well as for each type of subcortical ischemic lesion and risk factor. The grade of subcortical ischemic lesion was dichotomized as follows: grades 0 and 1 were assigned to those considered as early findings, while grades 2 and 3 were assigned to those considered as advanced findings. The ORs and 95% confidence intervals (CIs) were calculated using a logistic regression model. The contributing factors that were included in the logistic regression model were the conventional risk factors, the MRI findings for each subcortical ischemic lesion, and the 24-hour BP values. Correlations between the 24-hour BP values and the neuropsychological findings were analyzed using Pearson's correlation test adjusted for age and education level. Statistical analyses were

performed with SPSS (Windows version 13, SPSS, Chicago, IL, USA), using an alpha level of 0.05.

Results

General data

The initial sample comprised 123 patients: normal controls (*n*=34) and patients with SvMCI or SVaD (*n*=89). Some of the subjects were excluded due to 1) strategic infarction dementia (*n*=2), 2) psychiatric disorder (*n*=2), 3) a medical disease affecting their cognition (*n*=1), 4) severe hippocampal atrophy (*n*=2), 5) a heart disease such as myocardial infarction or atrial fibrillation (*n*=2), 6) midlife-onset hypertension (*n*=2), 7) a modified Rankin Scale score of ≥5 (*n*=1), or 8) MR-angiogram-proven severe large-vessel stenosis (*n*=2). This led to the final experimental cohort comprising 79 patients with SvMCI or SVaD, plus 30 normal controls. Of those with a subcortical vascular event, 37 were diagnosed as having SvMCI and 42 were diagnosed as having SVaD. The entire cohort of 109 subjects comprised 63 men and 46 women aged 69.9±4.12 years (range, 64-76 years). Table 1 lists the demographic data, conventional risk factors, and MRI findings for each subcortical-ischemic-lesion type, and the 24-hour BPs in the three study groups. None of the subject demographics differed significantly between the three groups.

Comparison of 24-hour blood pressure values in the subcortical vascular mild cognitive impairment, subcortical vascular dementia, and control groups

All BP values except for daytime DBP differed significantly between the three study groups. Multiple comparisons revealed that the daytime and nighttime SBPs were significantly higher in the SvMCI group than in the control group, and that the SBP variability and PP were significantly higher in the SVaD group than in the control group. The prevalence of the dipper type also differed markedly between the SVaD and control groups and between the SVaD and SvMCI groups (Table 2). Six patients (30%) in the control group exhibited a nondipper status, while 17 (45%) and 27 (65%) patients in the SvMCI and SVaD groups, respectively, exhibited a nondipper status; there were no hyperdippers.

Associations between subcortical vascular mild cognitive impairment and subcortical vascular dementia, and the conventional risk factors and 24-hour blood pressure values

The ORs for the risk factors of SVaD are presented in Table 3. They were greatest for PVH (OR, 1.95; 95% CI, 1.137-3.343) and DWH (OR, 1.80; 95% CI, 1.042-3.109). Moreover, there was a significant association between the nondipper type and presence of SVaD (OR, 4.827; 95% CI, 1.07-12.05).

Association between 24-hour blood pressure values and subcortical ischemic lesions

Table 4 lists the OR and 95% CI for each advanced subcortical ischemic lesion type, relative to the early-findings groups, for 24-hour BP values. High daytime SBP (OR, 3.032; 95% CI, 1.086-8.465), high nighttime SBP (OR, 3.538; 95% CI, 1.212-10.328), and absence of dipping (OR, 4.178; 95% CI, 1.830-8.826) were associated with PVH;

Table 1. Demographic and clinical characteristics of the subjects

	Study group			$p^{\dagger}$
	SvMCI (*n*=37)	SVaD (*n*=42)	Control (*n*=30)	
Age (years)	71.59±5.59	69.98±5.83	68.77±3.9	0.095
Education level (years)	5.41±3.18	6.35±4.47	6.24±3.14	0.495
Sex (M/F)	22/15	23/19	18/12	0.860
Hypertension	26 (70%)	34 (80%)	24 (80%)	0.802
Diabetes	13 (35%)	19 (45%)	9 (30%)	0.974
Hypercholesterolemia	11 (30%)	15 (35%)	6 (20%)	0.669
SM	7 (20%)	6 (15%)	9 (30%)	0.545
LVH	9 (25%)	15 (35%)	6 (20%)	0.692
Anti-HTN medication	22 (60%)	34 (80%)	21 (70%)	0.602
K-MMSE	22.06±5.04	19.19±4.14	28.27±1.04	0.000*
Grade of PVH	1.73±0.77	2.19±0.67	0.57±0.48	0.000*
Grade of DWH	1.62±0.64	2.29±0.60	0.20±0.76	0.000*
Grade of LI	1.00±0.71	0.96±0.70	0.16±0.79	0.000*

The data are mean±SD values or *n* (%). *p<0.05, †Calculated using ANOVA.
SvMCI: subcortical vascular mild cognitive impairment, SVaD: subcortical vascular dementia, HTN: hypertension, SM: smoking, LVH: left ventricular hypertrophy, LI: lacunar infarcts, PVH: periventricular hyperintensities, DWH: deep white-matter hyperintensity, K-MMSE: Korean adaptation of the Mini-Mental State Examination.

Table 2. Comparison of 24-hour blood pressure (BP) between the SvMCI, SVaD, and control groups

Variable	SvMCI (n=37)	SVaD (n=42)	Control (n=30)	p	Post hoc† (Tukey)
Daytime SBP	141.96±10.72	130.92±10.89	131.05±9.52	0.002*	SvMCI>control
Nighttime SBP	136.58±13.85	129.66±11.92	123.33±10.48	0.000*	SvMCI>control SvaD>control
Daytime DBP	88.07±7.95	84.38±7.79	82.21±4.40	0.109	
Nighttime DBP	84.04±9.81	82.95±9.3	78.15±7.83	0.031*	SvMCI>control
PP	53.54±10.55	56.96±10.30	46.34±5.14	0.000*	SVaD>control
SBP variability	13.60±4.80	15.71±3.4	12.37±3.8	0.047*	SVaD>control
Diurnal BP pattern					
Dipper	12 (33%)	7 (15%)	20 (65%)	0.000*	SVaD>SvMCI SvMCI>control
Nondipper	17 (45%)	27 (65%)	8 (30%)		
Reversed dipper	8 (22%)	8 (20%)	2 (5%)		

*p<0.05. SBP: systolic blood pressure, DBP: diastolic blood pressure, PP: pulse pressure.

Table 3. Odds ratios (ORs) and 95% confidence intervals (CIs) for the SvMCI/SVaD group for conventional risk factors and 24-hour values

Variable	OR	95% CI	p
Age (years)			
<70	1.0		
>70	1.833	0.907-3.704	0.091
Sex (M/F, reference: F)	1.274	0.6783-2.047	0.572
HTN	1.037	0.611-1.759	0.893
DM	1.067	0.527-2.157	0.857
LDL	1.20	0.518-2.777	0.670
SM	1.00	0.375-2.664	1.00
LVH	1.40	0.622-3.152	0.416
24-hour BP values			
Daytime SBP			
LG	1.00		
HG	0.833	0.490-1.417	0.501
Nighttime SBP			
LG	1.00		
HG	0.967	0.580-1.610	0.896
Nighttime DBP			
LG	1.00		
HG	1.097	0.674-1.784	0.782
BP dipping status			
Dipper	1.00		
Nondipper	4.827	1.07-12.05	0.039*
Reverse dipper	1.40	0.622-3.152	0.416
SBP variability			
LG	1.00		
HG	1.117	0.451-2.765	0.811
PP			
LG	1.00		
HG	1.254	0.579-4.21	0.710

*p<0.05. SvMCI: subcortical vascular mild cognitive impairment, SVaD: subcortical vascular dementia, HTN: hypertension, HG: high group, LG: low group, DM: diabetes mellitus, LDL: low-density lipoprotein cholesterol, BP: blood pressure, SBP: systolic blood pressure, DBP: diastolic blood pressure.

SBP variability was associated with DWH (OR, 3.375; 95% CI, 1.007-11.312).

Correlation between 24-hour blood pressure values and the results of neuropsychological testing

The age- and education-adjusted partial correlation analysis revealed that loss of dipping was significantly associated with reduced attention (r=0.267, p=0.019) and frontal executive dysfunction (r=0.348, p=0.002), and that SBP variability was significantly associated with reduced attention (r=-0.258, p=0.024), frontal executive dysfunction (r=-0.243, p=0.033), and visuospatial dysfunction (r=-0.305, p=0.007). PP was associated with reduced attention (r=-0.258, p=0.024)(Table 4).

Discussion

The main findings of this study are twofold: 1) the prevalence of disruption of the diurnal BP rhythm was higher in the patients with SvMCI or SVaD than in the controls, and was associated with cognitive dysfunction; and 2) the prevalence rates of high-grade SBP variability and increased PP were higher in patients with SVaD than in patients with SvMCI and in the controls.

Most previous studies found that hypertension was closely related to WML and cognition, and it is certain that the size of an ischemic WML is correlated with the SBP and cognitive impairment.[4,19-24] However, there is considerable controversy regarding the relationships between BP variability, ischemic WMLs, and cognition. It is noteworthy that van Boxtel et al.[14] systematically examined the relationships between BP, WMLs, and cognitive performance in the same cohort of hypertensive subjects with asymptomatic cerebrovascular damage, and found no conclusive evidence of a connection between diurnal BP variation and early target-organ damage in the brain, although the ABP profile may

Table 4. Age- and education-adjusted correlation between 24-hour BP values and scores in each cognitive domain of Neuropsychological Screening Battery (SNSB) tests in SvMCI/SVaD patients

SNSB test	Attention	Language function	Visuospatial function	Memory	Frontal executive function
Levels of 24-hour BP values					
Daytime SBP	-0.031	0.074	0.051	0.055	0.129
Nighttime SBP	-0.222	-0.063	-0.052	-0.148	-0.114
Daytime DBP	0.017	0.089	0.038	0.045	0.130
Nighttime DBP	-0.205	-0.043	-0.102	-0.188	-0.045
BP dip	0.267*	0.030	0.151	0.146	0.348**
PP	-0.258*	-0.171	0.046	0.076	-0.052
AASI	-0.043	-0.030	0.053	0.093	-0.018
SBP variability	-0.355**	0.055	-0.305**	-0.111	-0.243*

*p<0.05, **p<0.01.
AASI: Ambulatory Arterial Stiffness index, SBP: systolic BP, DBP: diastolic BP, BP: blood pressure, PP: pulse pressure.

have been predictive of the cerebral-lesion type. Very few studies have investigated the relationship between the dynamic changes in BP and subcortical ischemic VCI, including SvMCI and SVaD, in the same cohort of subjects.[25]

Previous studies employing ABP monitoring found that the mean SBP was higher in patients with SVaD than in controls, a finding that differs somewhat from those of the present study showing that the SBP was higher in the patients with SvMCI than in the control and SVaD groups.[26,27] However, the reason for these differences is unclear since the BP levels of the subjects in the present study were contaminated by antihypertensive medication. SBP variability and PP were significantly higher in the SVaD patients, indicating a possible association with the loss of vasomotor reactivity in advanced small-vessel lesions.

Many studies have found a close relationship between SBP variability and Binswanger's disease.[28,29] A high PP reflects increased arterial stiffness, and the penetrating cerebral arteries of hypertensive patients with high PP show lower responses to hypotension, increasing the risk of developing WMLs.[29] There is increasing evidence that elevated arterial stiffness increases the risk of cardiovascular complications.[30,31]

A recent notable finding related to 24-hour BP is the prominent loss of diurnal BP rhythm in Binswanger's disease.[26] The same researchers also found that nondippers were more prevalent in the SvMCI and SVaD groups than in the control group. The precise relationship between subcortical small-vessel lesions and loss of dipping is controversial, with some researchers (e.g., van Boxtel et al.)[14] suggesting that dipping status is unrelated to cerebral pathology. However, many other studies (including our own) have found that nondipping is closely related to possible hypertensive target-organ damage, and that nondipping and reverse-dipping statuses are more common in patients with subcortical small-vessel ischemia.[9,13,24,27] It was also found that reduced attention, visuospatial dysfunction, and frontal executive dysfunctions are related to loss of dipping.

The clinical manifestations of SVaD result from disruption to the subcortical-frontal systems, particularly the dorsolateral prefrontal-subcortical circuits.[33] The characteristic neuropsychological profile of cerebral small-vessel disease includes early attention and executive function impairment, with slowing of motor performance and information processing.[1] This has been confirmed in studies showing that subcortical gray- and white-matter hyperintensity volumes and scores on white-matter rating scales on MRI scans are significantly correlated with the degree of neuropsychological dysfunction in different patient populations. In addition, we showed that these cognitive dysfunctions in patients with SVaD were correlated with the changes in their diurnal BP rhythm.

The limitations of this study are 1) its relatively small sample, 2) the absence of a prospective follow-up investigation, and 3) the absence of established SvMCI criteria; it is possible that some of the patients in our cognitively impaired groups were suffering from amnestic MCI. However, we did attempt to exclude those patients with pure amnestic MCI by applying detailed neuropsychological testing, brain imaging, and history-taking.

To the best of our knowledge, the present study is the first to compare SvMCI and SVaD through ABP monitoring, and to analyze the relationships between 24-hour BP data, subcortical-ischemic-lesion types, and cognitive performance. Based on the results of this study, it is suggested that the ABP profile is related to the progression characteristics of subcortical small-vessel disease. The ABP profile might be predictive of the progression of subcortical WML in patients with subcortical VCI, which suggests that BP control should be considered as a wide-ranging target for the prevention of SVaD. Modulating the loss of dipping and the increase in SBP variability and PP in SvMCI patients could help prevent advanced subcortical small-vessel disease, while simultaneously lowering the BP.

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