Ambulatory Versus Home Versus Clinic Blood Pressure
The Association With Subclinical Cerebrovascular Diseases:
The Ohasama Study

Azusa Hara, Kazushi Tanaka, Takayoshi Ohkubo, Takeo Kondo, Masahiro Kikuya, Hirohito Metoki, Takanao Hashimoto, Michihiro Satoh, Ryusuke Inoue, Kei Asayama, Taku Obara, Takuo Hirose, Shin-Ichi Izumi, Hiroshi Satoh, Yutaka Imai

See Editorial Commentary, pp 2–4

Abstract—The usefulness of ambulatory, home, and casual/clinic blood pressure measurements to predict subclinical cerebrovascular diseases (silent cerebrovascular lesions and carotid atherosclerosis) was compared in a general population. Data on ambulatory, home, and casual/clinic blood pressures and brain MRI to detect silent cerebrovascular lesions were obtained in 1007 subjects aged ≥55 years in a general population of Ohasama, Japan. Of the 1007 subjects, 583 underwent evaluation of the extent of carotid atherosclerosis. Twenty-four–hour, daytime, and nighttime ambulatory and home blood pressure levels were closely associated with the risk of silent cerebrovascular lesions and carotid atherosclerosis (all \( P < 0.05 \)). When home and one of the ambulatory blood pressure values were simultaneously included in the same regression model, each of the ambulatory blood pressure values remained a significant predictor of silent cerebrovascular lesions, whereas home blood pressure lost its predictive value. Of the ambulatory blood pressure values, nighttime blood pressure was the strongest predictor of silent cerebrovascular lesions. The home blood pressure value was more closely associated with the risk of carotid atherosclerosis than any of the ambulatory blood pressure values when home and one of the ambulatory blood pressure values were simultaneously included in the same regression model. The casual/clinic blood pressure value had no significant association with the risk of subclinical cerebrovascular diseases. Although the clinical indications for ambulatory blood pressure monitoring and home blood pressure measurements may overlap, the clinical significance of each method for predicting target organ damage may differ for different target organs. (Hypertension. 2012;59:22-28.)

Key Words: home blood pressure ■ ambulatory blood pressure ■ casual/clinic blood pressure ■ silent cerebrovascular lesions ■ carotid atherosclerosis ■ general population

Elevated blood pressure (BP) is a strong, independent risk factor for incident cardiovascular diseases.\(^1\) The recent international hypertension management guidelines\(^2\)-\(^4\) confer increasing weight to methods of measuring BP outside the medical environment. 24-hour ambulatory BP (ABP) measurements, self-measurements at home (HBP), or both. Indeed, many studies have demonstrated their relationship with target organ damage\(^5\)-\(^10\) and their prognostic values for cardiovascular diseases.\(^11\)-\(^15\)

There have been a few small studies that directly compared the usefulness of these 2 measurement methods. Overall, these data suggested that ABP and HBP are equally reliable for predicting target organ damage,\(^16\)-\(^18\) that ABP is strongly associated with target organ damage,\(^19\) and that HBP has a closer association with target organ damage.\(^20\) However, there are still insufficient data comparing the predictive values for target organ damage of ABP, HBP, and casual/clinic BP (CBP), especially for subclinical cerebrovascular diseases, such as silent cerebrovascular lesions (SCLs) or carotid atherosclerosis.

SCLs, seen as white matter hyperintensities and lacunar infarcts, which are frequently observed on MRI scans in elderly individuals, constitute an independent predictor of the risk of symptomatic stroke\(^21\) and are associated with cogni-
tive impairment or dementia.\textsuperscript{22} Carotid atherosclerosis (carotid intima-media thickness and plaques) more accurately predicts the risk of future myocardial infarction and stroke than traditional risk factors.\textsuperscript{23,24}

The objective of this study was to compare the usefulness of ABP monitoring, HBP measurements, and CBP measurements for the prediction of subclinical cerebrovascular diseases in a general Japanese population.

**Methods**

**Design**

This study was a part of the Ohasama Study, a community-based project to measure ABP and HBP. The socioeconomic and demographic characteristics of this region and the full details of the project have been described elsewhere.\textsuperscript{25,26} The study protocol was approved by the institutional review board of Tohoku University School of Medicine (Sendai, Japan) and by the Department of Health of the Ohasama Town Government.

**Study Population**

Of the 2400 eligible individuals aged \( \geq 55 \) years; 1007 subjects (42.0%; mean age 66.3±5.8 years; 67.4% women) gave informed consent; had ABP, HBP, and CBP measurements; completed MRI; and provided details of their medical histories and cardiovascular risk factors. Of the 1007 subjects, 583 underwent carotid ultrasound examination for further evaluation of the extent of carotid atherosclerosis. The details of the selection and the representativeness of study subjects are described in the online Data Supplement (please see http://hyper.ahajournals.org).

**Subclinical Cerebrovascular Diseases**

The evaluations of SCLs and carotid atherosclerosis are described in the online Data Supplement.

**BP Measurements**

ABP monitoring was performed using the ABPM-630 (Nippon Colin, Komaki, Japan),\textsuperscript{27} a fully automatic device that uses the cuff-oscillometric method to measure BP, which was preset to measure BP every 30 minutes. According to the diary, “daytime” and “nighttime” were determined as periods of being awake and asleep, respectively. The mean (±SD) number of total ABP measurements was 43.6±4.9 (daytime: 28.3±4.7; nighttime: 15.3±2.8).

HBP was measured with the HEM701C (Omron Healthcare Co. Ltd, Kyoto, Japan), a semiautomatic device based on the cuff-oscillometric method.\textsuperscript{28} The subjects were asked to measure their BP every morning and evening\textsuperscript{29} and to record the results over a 4-week period. The mean (±SD) number of HBP measurements was 49.0±11.3 (morning: 24.7±5.7; evening: 24.2±6.2).

At the time of MRI and carotid ultrasound examination, a physician measured the CBP twice consecutively with the participant sitting after an interval of rest of \( \geq 2 \) minutes using a mercury sphygmomanometer or an automatic device (HEM907, Omron Healthcare Co. Ltd.). The average of the 2 readings was defined as the CBP.

Each subject had ABP, HBP, and CBP measurements within a year. Details of BP measurements are described in the online Data Supplement.

**Biochemical Examination**

The biochemical examinations and the definitions of cardiovascular diseases, hypercholesterolemia, and diabetes mellitus in the Ohasama Study have been reported previously.\textsuperscript{5–7,30}

**Data Analysis**

The analyses of the data in the present study are described in the online Data Supplement.

### Table. Population Characteristics and the Association Between SCLs and Cardiovascular Risk Factors

<table>
<thead>
<tr>
<th>Variables</th>
<th>SCLs (−)</th>
<th>SCLs (+)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>501</td>
<td>506</td>
<td>0.03</td>
</tr>
<tr>
<td>Men, %</td>
<td>29</td>
<td>36</td>
<td>0.03</td>
</tr>
<tr>
<td>Age, y</td>
<td>64±5</td>
<td>68±6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BMI, kg/m(^2)</td>
<td>24±3</td>
<td>23±3</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Blood pressure, mm Hg

<table>
<thead>
<tr>
<th>Ambulatory</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>24-h</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>123±12</td>
<td>128±12</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diastolic</td>
<td>72±7</td>
<td>74±7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Daytime</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>129±13</td>
<td>134±13</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diastolic</td>
<td>76±8</td>
<td>78±8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Nighttime</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>111±13</td>
<td>117±14</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diastolic</td>
<td>63±7</td>
<td>66±8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Home</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>122±14</td>
<td>128±14</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diastolic</td>
<td>73±9</td>
<td>76±9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Casual/Clinic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>139±20</td>
<td>142±20</td>
<td>0.06</td>
</tr>
<tr>
<td>Diastolic</td>
<td>78±11</td>
<td>78±10</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Smoker, %           | 17       | 21       | 0.1   |

Drinker, %          | 28       | 28       | 0.97  |

Antihypertensive medication, % | 27 | 52 | <0.0001 |

Hypercholesterolemia, % | 36 | 36 | 0.9 |

Diabetes mellitus, % | 13 | 17 | 0.1 |

Atrial fibrillation, % | 2 | 4 | 0.1 |

Cardiovascular diseases, % | 9 | 16 | 0.001 |

Values are shown as mean±SD or percentage. SCL indicates silent cerebrovascular disease; BMI, body mass index.

### Results

**Risk of SCLs**

The characteristics of the study subjects and the associations between the risk factors and SCLs are presented in the Table. A total of 506 subjects (50%) had SCLs. The presence of SCLs was associated with older age, lower body mass index, a higher percentage of men, antihypertensive medication, and cardiovascular diseases (all \( P<0.05 \)). The subjects with SCLs had higher ABP and HBP levels (all \( P\leq0.0001 \)).

On multiple logistic regression analyses adjusted for the possible confounding factors, 24-hour, daytime, nighttime ambulatory systolic BP (SBP), and home SBP values were significantly associated with the risk of SCLs, whereas casual/clinic SBP values had no association with the risk of SCLs (Figure 1). However, when home SBP and one of the ambulatory SBP values were simultaneously included in the same regression model, the home SBP value was not significantly associated with the risk of SCLs, whereas ambulatory SBP values remained a significant predictor (Figure 2). Of the
ambulatory SBP values, the nighttime SBP value was more strongly associated with the risk of SCLs than the daytime SBP value (Figure 2).

Casual/clinic SBP values had no significant association with the risk of SCLs when one of the ambulatory or home SBP values was simultaneously included in the same logistic regression model (Figure S1 in the online Data Supplement). Similar trends were observed when the risk for either white matter hyperintensities or lacunar infarcts was evaluated (Figures S2 and S3, respectively). The results for the risk of SCLs among the 583 subjects with carotid ultrasonography data were similar to those obtained for all 1007 subjects (Figure S4).

**Risk of Carotid Atherosclerosis**

Then, the associations among several ABP, HBP, and CBP values and carotid atherosclerosis were compared. The associations between cardiovascular risk factors and the presence of carotid atherosclerosis are presented in Table S2. Similar to SCLs, the subjects with carotid atherosclerosis had higher ambulatory and home BP levels than those without (all P<0.05), except for daytime diastolic BP (P=0.07).

In the logistic regression analysis, several ambulatory and home SBP values were significantly associated with the risk of carotid atherosclerosis, whereas the casual/clinic SBP value was not (Figure 3). When home SBP and one of the ambulatory SBP values were simultaneously included in the same regression model, the home SBP value was more strongly associated with carotid atherosclerosis than any of the ambulatory SBP values (Figure 4). Of the ambulatory SBP values, daytime and nighttime SBP values were similarly associated with the risk of carotid atherosclerosis (Figure 4).

Casual/clinic SBP values had no significant associations with the risk of carotid atherosclerosis when one of the ambulatory or home SBP values was simultaneously included in the same logistic regression model (Figure S5).

When ambulatory and home diastolic BP values were entered into this model instead of SBP values, all of the ambulatory and home diastolic BP values were similarly associated with the risk of subclinical cerebrovascular diseases (Figure S6 for SCLs and Figure S7 for carotid atherosclerosis).

In stratified analyses by antihypertensive treatment, similar results were more clearly observed among treated subjects,
although there were no significant interactions (all P values for interaction: >0.1; Figure S8 and S9 for SCLs among untreated subjects; Figure S10 and S11 for SCLs among treated subjects; Figure S12 and S13 for carotid atherosclerosis among untreated subjects; and Figure S14 and S15 for carotid atherosclerosis among treated subjects).

When one of morning pressor surges in BP, nocturnal decline, or BP variability was included in the regression model one at a time, there was a significant association only between nighttime SBP variability and the risk of carotid atherosclerosis (Figure S16 for SCLs and Figure S17 for carotid atherosclerosis). However, when the nighttime SBP value was simultaneously included in the same regression model, nighttime SBP variability did not remain significantly associated (Figure S18).

There were no significant associations between casual/clinic, home, and any ambulatory heart rate values and the risk of subclinical cerebrovascular diseases for the subjects without a history of cardiovascular diseases (Figure S19 for SCLs and Figure S20 for carotid atherosclerosis).

Similar results were obtained when HBP values averaged over 7 days of measurements (with the exception of the first day) in accordance with a guideline of the European Society of Hypertension and one of the ABP or CBP values was included in the same multiple logistic regression model (Figure S21 for SCLs and Figure S22 for carotid atherosclerosis).

**Discussion**

To the best of our knowledge, this is the first study to compare ABP, HBP, and CBP values for their associations with the risk of subclinical cerebrovascular diseases in a large general population. ABP monitoring and HBP measurements have several advantages over CBP measurements, the absence of the white-coat effect, the lack of digit preference and observer bias when automated devices are used, and better correlation to target organ damage and prognosis.

Notwithstanding the above similarities, there are major differences in the characteristics between ABP monitoring and HBP measurements.

One of the advantages of ABP monitoring is its ability to provide a series of frequent and automated BP measurements throughout a 24-hour period. This might have clinical implications in light of the evidence supporting the adverse
prognostic relevance of specific patterns of BP variability over 24 hours. On the other hand, HBP measurements have been reported to provide more reliable and reproducible BP information, because they allow multiple measurements under controlled conditions and avoid the placebo effect.

There have been a few direct comparisons between ABP monitoring and HBP measurements with respect to the association with target organ damage, but the results were controversial. The degree of association between left ventricular hypertrophy assessed by echocardiography and ABP or HBP is comparable. In one study, ABP was more closely associated with left ventricular mass index and left ventricular wall thickness. Another study showed that left ventricular mass was associated more strongly with HBP than with ABP. For different markers of target organ damage, including urinary albumin excretion and carotid intima-media thickening, ABP measurements showed a comparable degree of association for ABP and HBP. However, these results are based on a small series, and a large population sample has not yet been studied. With respect to the association of ABP and HBP values with the risk of SCLs, no data are available. In this relatively large population study, the nighttime ABP value was the strongest predictor of SCLs, whereas the HBP value was more strongly associated with the risk of carotid atherosclerosis than any of the ABP values.

In the present study, the nighttime BP value had the strongest association with SCLs. Normally, BP falls during sleep and rises in the waking hours. It is possible that a high BP at nighttime promotes the development of SCLs. Several reports have demonstrated the association between SCLs and clinical conditions that cause nighttime hypertension, such as activation of the renin-angiotensin system, salt-sensitive hypertension, and the sleep apnea syndrome. These conditions might mediate the association between the nighttime BP value and the risk of SCLs in the present study. However, the cross-sectional design of the present study did not allow us to clarify cause-and-effect relationships.

It was demonstrated that the HBP value had the strongest association with the risk of carotid atherosclerosis. It has been shown previously that ABP has poorer reproducibility than HBP. The present result, that the HBP value had the strongest association with the risk of carotid atherosclerosis, suggests that carotid atherosclerosis may be affected by the continuous and stable stress of BP. However, we have also reported previously that carotid plaque was associated with not only BP itself but also with BP variability. Further studies are required to clarify the associations of BP levels, day-by-day variability, and circadian BP variation with the risk of carotid atherosclerosis.

In the present study, means of 44 (daytime: 28; nighttime: 15) ABP measurements, 49 HBP measurements, and 2 CBP measurements were obtained. It is possible that such a number of measurements may be responsible for the strong association with subclinical cerebrovascular diseases that was found. However, the nighttime BP value taken as an average of 15 measurements was the strongest predictor for SCLs, and the HBP value of 49 measurements was the strongest one for carotid atherosclerosis in the present study. Furthermore, when HBP values averaged over 7 days of measurements (with the exception of the first day) in accordance with the European Society of Hypertension guideline and one of the ABP or CBP values was included in the same multiple logistic regression model, BP values were similarly associated with the risk of subclinical cerebrovascular diseases. As for the number of CBP measurements, we compared previously the predictive value of CBP and HBP values using the same or fewer measurements (1 or 2 measurements) and showed that HBP had a stronger predictive power than CBP, even when fewer measurements were used. We also reported that HBP was more closely associated with the risk of SCLs or carotid atherosclerosis than CBP using the same number of HBP measurements (2 measurements) as for the CBP. These results suggest that not only the number, duration, or intensiveness of measurements, but other factors that have already been described above, may be associated with the superior predictive power of nighttime BP and HBP.

The possibility of selection bias needs to be considered when generalizing the present findings, because the participation rate of the study population was only 42.0%. Furthermore, it is possible that 424 high-risk subjects might have been excluded in the analysis examining the associations with carotid atherosclerosis, because the 424 subjects without carotid ultrasonography data had a higher risk than those with the data. Meanwhile, the casual/clinic SBP level was significantly higher in the 583 subjects with carotid ultrasonography data. There might be selection bias in the excluded 424 subjects without carotid ultrasonography data, although the results for the risk of SCLs among the 583 subjects with carotid ultrasonography data were similar to those of all 1007 subjects. In addition, our conclusions about HBP are applicable only when HBP is measured using a similar scheme. Furthermore, marked differences exist in the epidemiology of cardiovascular diseases between Japan and the United States or European countries. Thus, further research involving other ethnic and cultural populations is needed to confirm the generalizability of the findings in the present study.

Perspectives
The findings of the present study suggest that the nighttime ABP value is the strongest predictor for SCLs, whereas the HBP value is the strongest predictor for carotid atherosclerosis among several ABP, HBP, and CBP values. Further prospective studies that directly compare the use of ABP, HBP, and CBP values for predicting associated target organ damage and prognosis are necessary. Both ABP monitoring and HBP measurements are extremely useful for determining hypertensive cardiovascular diseases. Although the clinical indications for ABP monitoring and HBP measurements may overlap, the clinical significance of each method for predicting target organ damage may differ among different target organs.

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Disclosures

None.

References

27. Imay Y, Otsuka K, Kawano Y, Shimada K, Hayashi H, Tochikubo O, Miyakawa K, Fukiyama K. Japanese Society of Hypertension (JSH) Ambulatory vs Home vs Clinic Blood Pressure


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Supplemental Methods

Study population

The details of the selection of study subjects have been described previously \(^1\,^2\). In 1998, the total population of Ohasama was 7,202. Of these inhabitants, 3,077 were 55 years of age or over. People who were hospitalized, mentally ill, or bedridden were excluded from the study (n = 185). People who worked outside of the town were also excluded (n = 492), since our project included ambulatory blood pressure (ABP) measurements, and public health nurses needed to visit the subjects to attach a device for ABP monitoring on working days. Of the remaining 2,400 eligible individuals, 1,007 subjects (42.0%, mean age 66.3±5.8 years, 67.4% women) gave informed consent, had ABP, home blood pressure (HBP), and casual/clinic blood pressure (CBP) measurements, completed magnetic resonance imaging (MRI), and provided details of their medical histories and cardiovascular risk factors. Of the 1,007 subjects, 583 underwent further evaluation of the extent of carotid atherosclerosis using carotid ultrasound examination. Age, ambulatory systolic blood pressure (SBP), and the proportions on antihypertensive treatment and having a history of cardiovascular diseases were significantly lower, and casual/clinic SBP and diastolic blood pressure (DBP) and the proportion having a history of hypercholesterolemia were significantly higher in the 583 study subjects with carotid ultrasonography data than in the 424 subjects without it, as tabulated in the Supplemental Table (Table S1).

Silent Cerebrovascular Lesions (SCLs)

MRI was performed using a superconducting magnet with a main 0.5-T coil \(^3\,^4\,^5\). The brain was imaged in the axial plane in 10-mm-thick slices, and T1- and T2-weighted images were collected. A lacunar infarct was defined as an area of low signal intensity measuring ≤15 mm and ≥3 mm on T1-weighted images and that was visible as a hyperintense lesion on T2-weighted images. Hyperintense punctate lesions evident only on the T2-weighted images were not counted as lacunar infarcts. White matter hyperintensity (WMH) was defined as hyperintensity only on T2-weighted images, and was graded according to Fazekas \(^6\) as follows: absent (grade 0), punctate (grade 1), early confluent (grade 2), and confluent (grade 3). Small caps (<5×10 mm) on the horns of the lateral ventricles and pencil-thin lining around the ventricles were considered normal. Larger caps (≥5×10 mm) were considered grade 2.

A neurosurgeon and four technical experts directed by the neurosurgeon independently evaluated the MRI findings in a blinded manner \(^3\,^4\,^5\). In the case of disagreement, a consensus reading was held. Both intra-reader and inter-reader studies (n = 111) showed good agreement. Kappa statistics were between 0.68 and 0.86 for lacunar infarct, and between 0.72 and 0.86 for WMHs. SCLs were defined as
white matter hyperintensities of grade 1 or more, the presence of lacunar infarcts, or any combination of these findings.

Carotid atherosclerosis

Carotid ultrasound was performed using a real-time, B-mode ultrasound imaging unit (Toshiba Sonolayer SSA-250A; Toshiba, Tokyo, Japan) with a 7.5-MHz annular array probe giving an axial resolution of 0.25 mm. The ultrasound examination was performed by specially trained physicians using a standardized technique. They were blinded with respect to the individuals’ characteristics. The study procedure involved scanning the near and far walls of both common carotid arteries, approximately 1 cm proximal to the carotid bulb in the longitudinal view. During each examination, different scanning angles (anterior, lateral, and posterior) were used to identify the maximum intima-media thickness (IMT) in each wall. Mean IMT was defined as the mean of the maximum wall thickness for the near and far walls of both the left and the right common carotid arteries. The common carotid artery, carotid bifurcation, internal carotid artery, and external carotid artery were examined on both sides for the presence of plaques, defined as a focal widening relative to adjacent segments, with protrusion into the lumen composed either of calcified deposits alone or the presence of a combination of calcified and non-calcified material. All participants were examined in the sitting position.

The reproducibility of the IMT measurements was assessed in 29 individuals. The within-observer coefficient of variation for the mean IMT between the first and second observations was 6.3% (mean±SD of the difference 0.035±0.035 mm). The coefficient of variation between two observers was 11.9% (mean±SD of the difference 0.085±0.062 mm), indicating that the reproducibility of the IMT measurement was comparable to that seen in other studies.

Carotid atherosclerosis was defined as carotid mean IMT measuring more than 0.9 mm or the presence of focal carotid plaque.

Blood pressure (BP) measurements

ABP monitoring was performed using the ABPM-630 (Nippon Colin, Komaki, Japan), a fully automatic device that uses the cuff-oscillometric method to measure BP, which was preset to measure BP every 30 min. The device was attached by well-trained public health nurses who visited the participants’ homes on a weekday morning and detached the device the next morning. The participants were asked to report their daily activities, including the time they went to bed and the time they got up. According to the diary, ‘daytime’ and ‘nighttime’ were determined as periods of being awake and asleep, respectively. Artifactual measurements during recordings were defined according to previously described criteria and were omitted from the
analysis. The mean (±SD) number of total ABP measurements was 43.6±4.9 (daytime, 28.3±4.7; nighttime, 15.3±2.8).

HBP was measured with the HEM701C (Omron Healthcare Co. Ltd, Kyoto, Japan), a semi-automatic device based on the cuff-oscillometric method 17, which generates a digital display of both SBP and DBP.

Physicians and/or public health nurses taught subjects how to take the HBP measurements. The subjects were asked to measure their BP every morning within 1 h of waking in the sitting position after an interval of rest of more than 2 min, and to record the results over a 4-week period. Subjects on antihypertensive drugs measured their BP before taking their medication. During a 4-week period, subjects were also asked to measure their BPs once in the evening just before going to bed. Subjects were allowed to measure their own BP two or more times and asked to record all measurements on the worksheet on each occasion, though only the first measurement value on each occasion was used for averaging and for evaluation of HBP to exclude selection bias by the participants 18. The average of all HBP measurements was used because it was more closely associated with SCLs than those of morning HBP or evening HBP measurements in our previous study 3. The mean (±SD) number of HBP measurements was 49.0±11.3 (morning, 24.7±5.7; evening, 24.2±6.2).

At the time of MRI and carotid ultrasound examination, a physician measured the CBP twice consecutively with the participant sitting after an interval of rest of more than 2 min using a mercury sphygmomanometer or an automatic device (HEM907, Omron Healthcare Co. Ltd.). CBP measurements were taken during the daytime from 10:00 to 13:00 or from 14:00 to 16:00. The average of the two readings was defined as the CBP.

Each subject had ABP, HBP, and CBP measurements within a year.

The ABP, HBP, and CBP measuring devices used in the present study had been validated previously 16, 17, 19 and met the criteria of the Association for the Advancement of Medical Instrumentation 20.

Data Analysis

Short-term BP variability during the daytime and nighttime, calculated as the SD of daytime and nighttime ABP, respectively, was examined. We have previously demonstrated that the magnitude of the nocturnal decline in BP was the strongest determinant of the SD of 24-h BP, indicating that the SD of 24-h BP is not an appropriate index of short-term BP variability 21. The percentage decline in nocturnal BP was calculated as (daytime BP – nighttime BP)*100/daytime BP 22, 23. The amplitude of the morning pressor surge was calculated as (2-h average of BP after waking) – (2-h average of BP before waking) 23.
The cardiovascular risk factors and several BP values (ABP, HBP, and CBP) of the subjects with and without each of the subclinical cerebrovascular diseases were compared by Student’s t-test or the χ²-test. Logistic regression models were used to examine the associations between several BP values and the risk of subclinical cerebrovascular diseases adjusted for cardiovascular risk factors. To compare the associations among several BP values and the risk of SCLs, as well as carotid atherosclerosis, HBP, CBP, or one of the ABP values was simultaneously included in the same regression model. ABP, HBP, and CBP were not highly correlated (Spearman’s rank correlation coefficient for systolic BP; ABP and HBP: r = 0.60 to 0.67; ABP and CBP: r = 0.34 to 0.41; HBP and CBP: r = 0.47) and had a low degree of multicollinearity (variance inflation factor [VIF] 1.31 to 2.15 when both variables were included in the same model).

SAS software version 9.1 (SAS Institute Inc, Cary, NC, USA) was used for all statistical analyses. For all analyses, a two-tailed p <0.05 was considered significant.
References


Table S1: Background comparison between the subjects with data of carotid ultrasonography and those without it

<table>
<thead>
<tr>
<th>Variables</th>
<th>Without data of carotid ultrasonography</th>
<th>With data of carotid ultrasonography</th>
<th>P</th>
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<tbody>
<tr>
<td>Number of subjects</td>
<td>424</td>
<td>583</td>
<td></td>
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<tr>
<td>Men, %</td>
<td>35</td>
<td>31</td>
<td>0.1</td>
</tr>
<tr>
<td>Age, year</td>
<td>68 ± 5</td>
<td>65 ± 6</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>23 ± 3</td>
<td>24 ± 3</td>
<td>0.1</td>
</tr>
<tr>
<td>Blood pressure, mmHg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ambulatory</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24-h</td>
<td>Systolic 127 ± 13</td>
<td>124 ± 13</td>
<td>0.0008</td>
</tr>
<tr>
<td></td>
<td>Diastolic 73 ± 7</td>
<td>73 ± 7</td>
<td>0.2</td>
</tr>
<tr>
<td>Daytime</td>
<td>Systolic 133 ± 14</td>
<td>130 ± 14</td>
<td>0.0003</td>
</tr>
<tr>
<td></td>
<td>Diastolic 78 ± 8</td>
<td>77 ± 8</td>
<td>0.08</td>
</tr>
<tr>
<td>Nighttime</td>
<td>Systolic 116 ± 14</td>
<td>113 ± 14</td>
<td>0.007</td>
</tr>
<tr>
<td></td>
<td>Diastolic 65 ± 8</td>
<td>65 ± 8</td>
<td>0.5</td>
</tr>
<tr>
<td>Home</td>
<td>Systolic 126 ± 13</td>
<td>125 ± 15</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>Diastolic 75 ± 9</td>
<td>75 ± 9</td>
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</tr>
<tr>
<td>Casual/clinic</td>
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<td>144 ± 21</td>
<td>&lt;.0001</td>
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<td></td>
<td>Diastolic 76 ± 10</td>
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<tr>
<td>Smoker, %</td>
<td>20</td>
<td>18</td>
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<td>Drinker, %</td>
<td>25</td>
<td>29</td>
<td>0.2</td>
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<td>Antihypertensive medication, %</td>
<td>45</td>
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<td>25</td>
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<tr>
<td>Diabetes, %</td>
<td>17</td>
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<td>0.1</td>
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<tr>
<td>Atrial fibrillation, %</td>
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<td>2</td>
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<tr>
<td>Cardiovascular diseases, %</td>
<td>17</td>
<td>9</td>
<td>0.0002</td>
</tr>
<tr>
<td>Silent cerebrovascular diseases, %</td>
<td>58</td>
<td>45</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

Values are shown as mean ± SD or percent.

BMI: body mass index
<table>
<thead>
<tr>
<th>Variables</th>
<th>Carotid atherosclerosis</th>
<th>Carotid atherosclerosis</th>
<th>P</th>
</tr>
</thead>
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<tr>
<td></td>
<td>(−)</td>
<td>(+)</td>
<td></td>
</tr>
<tr>
<td>Number of subjects</td>
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<td>210</td>
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<tr>
<td>Men, %</td>
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<td>37</td>
<td>0.009</td>
</tr>
<tr>
<td>Age, year</td>
<td>64 ± 5</td>
<td>68 ± 6</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>24 ± 3</td>
<td>23 ± 3</td>
<td>0.009</td>
</tr>
<tr>
<td>Blood pressure, mmHg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ambulatory</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24-h</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>122 ± 12</td>
<td>128 ± 13</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Diastolic</td>
<td>72 ± 7</td>
<td>73 ± 7</td>
<td>0.03</td>
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<tr>
<td>Daytime</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>128 ± 13</td>
<td>134 ± 13</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Diastolic</td>
<td>76 ± 8</td>
<td>77 ± 8</td>
<td>0.07</td>
</tr>
<tr>
<td>Nighttime</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>111 ± 13</td>
<td>117 ± 14</td>
<td>&lt;.0001</td>
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<td>Diastolic</td>
<td>64 ± 7</td>
<td>66 ± 8</td>
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<tr>
<td>Home</td>
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<td></td>
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<tr>
<td>Systolic</td>
<td>122 ± 14</td>
<td>129 ± 15</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Diastolic</td>
<td>74 ± 9</td>
<td>76 ± 9</td>
<td>0.02</td>
</tr>
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<td>Casual/</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinic</td>
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<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>142 ± 21</td>
<td>147 ± 21</td>
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<tr>
<td>Diastolic</td>
<td>80 ± 11</td>
<td>78 ± 11</td>
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</tr>
<tr>
<td>Smoker, %</td>
<td>16</td>
<td>22</td>
<td>0.08</td>
</tr>
<tr>
<td>Drinker, %</td>
<td>28</td>
<td>32</td>
<td>0.3</td>
</tr>
<tr>
<td>Antihypertensive medication, %</td>
<td>29</td>
<td>47</td>
<td>&lt;.0001</td>
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<tr>
<td>Hypercholesterolemia, %</td>
<td>46</td>
<td>41</td>
<td>0.3</td>
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<tr>
<td>Diabetes, %</td>
<td>10</td>
<td>20</td>
<td>0.0009</td>
</tr>
<tr>
<td>Cardiovascular diseases, %</td>
<td>6</td>
<td>15</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

Values are shown as mean ± SD or percent.

BMI: body mass index
**Figure S1.** Odds ratios (ORs) and 95% confidence intervals (CIs) for the risk of silent cerebrovascular lesions per 1-SD increase in systolic blood pressure (SBP) when casual/clinic blood pressure and one of the ambulatory blood pressure or home blood pressure values are included in the same multiple logistic regression model. Adjusted for age, sex, body mass index, smoking status, drinking status, antihypertensive medication, and history of cardiovascular diseases, atrial fibrillation, hypercholesterolemia, or diabetes. The solid squares are centered on the point estimate, and the horizontal lines extending from squares represent 95% CIs.
Figure S2. Odds ratios (ORs) and 95% confidence intervals (CIs) for the risk of white matter hyperintensity per 1-SD increase in systolic blood pressure (SBP) when one of the ambulatory blood pressure and home blood pressure values are included in the same multiple logistic regression model. 

Adjusted for age, sex, body mass index, smoking status, drinking status, antihypertensive medication, and history of cardiovascular diseases, atrial fibrillation, hypercholesterolemia, or diabetes. The solid squares are centered on the point estimate, and the horizontal lines extending from squares represent 95% CIs.
SBP per 1-SD increase

<table>
<thead>
<tr>
<th>SBP per 1-SD increase</th>
<th>OR and 95%CI</th>
<th>Percentage increase in risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambulatory 24-h Home</td>
<td>26% (4% to 54%)</td>
<td>9% (-12% to 35%)</td>
</tr>
<tr>
<td>Ambulatory daytime Home</td>
<td>21% (-1% to 46%)</td>
<td>12% (-9% to 38%)</td>
</tr>
<tr>
<td>Ambulatory nighttime Home</td>
<td>26% (5% to 52%)</td>
<td>11% (-9% to 35%)</td>
</tr>
<tr>
<td>Ambulatory daytime</td>
<td>12% (-9% to 38%)</td>
<td>23% (-1% to 52%)</td>
</tr>
</tbody>
</table>

Figure S3. Odds ratios (ORs) and 95% confidence intervals (CIs) for the risk of lacunar infarction per 1-SD increase in systolic blood pressure (SBP) when one of the ambulatory blood pressure and home blood pressure values are included in the same multiple logistic regression model. Adjusted for age, sex, body mass index, smoking status, drinking status, antihypertensive medication, and history of cardiovascular diseases, atrial fibrillation, hypercholesterolemia, or diabetes. The solid squares are centered on the point estimate, and the horizontal lines extending from squares represent 95% CIs.
Figure S4. Odds ratios (ORs) and 95% confidence intervals (CIs) for the risk of silent cerebrovascular lesions per 1-SD increase in systolic blood pressure (SBP) when one of the ambulatory blood pressure and home blood pressure values are included in the same multiple logistic regression model for the 583 subjects with carotid ultrasonography data. Adjusted for age, sex, body mass index, smoking status, drinking status, antihypertensive medication, and history of cardiovascular diseases, atrial fibrillation, hypercholesterolemia, or diabetes. The solid squares are centered on the point estimate, and the horizontal lines extending from squares represent 95% CIs.
Figure S5. Odds ratios (ORs) and 95% confidence intervals (CIs) for the risk of carotid atherosclerosis per 1-SD increase in systolic blood pressure (SBP) when casual/clinic blood pressure and one of the ambulatory blood pressure or home blood pressure values are included in the same multiple logistic regression model. Adjusted for age, sex, body mass index, smoking status, drinking status, antihypertensive medication, and history of cardiovascular diseases, hypercholesterolemia, or diabetes. The solid squares are centered on the point estimate, and the horizontal lines extending from squares represent 95%CIs.
Figure S6. Odds ratios (ORs) and 95% confidence intervals (CIs) for the risk of silent cerebrovascular lesions per 1-SD increase in diastolic blood pressure (DBP) when one of the ambulatory blood pressure and home blood pressure values are included in the same multiple logistic regression model Adjusted for age, sex, body mass index, smoking status, drinking status, antihypertensive medication, and history of cardiovascular diseases, atrial fibrillation, hypercholesterolemia, or diabetes. The solid squares are centered on the point estimate, and the horizontal lines extending from squares represent 95%CIs.
Figure S7. Odds ratios (ORs) and 95% confidence intervals (CIs) for the risk of carotid atherosclerosis per 1-SD increase in diastolic blood pressure (DBP) when one of the ambulatory blood pressure and home blood pressure values are included in the same multiple logistic regression model Adjusted for age, sex, body mass index, smoking status, drinking status, antihypertensive medication, and history of cardiovascular diseases, hypercholesterolemia, or diabetes. The solid squares are centered on the point estimate, and the horizontal lines extending from squares represent 95%CIs.
Figure S8. Odds ratios (ORs) and 95% confidence intervals (CIs) for the risk of silent cerebrovascular lesions per 1-SD increase in systolic blood pressure (SBP) for subjects with no antihypertensive medications. Adjusted for age, sex, body mass index, smoking status, drinking status, and history of cardiovascular diseases, atrial fibrillation, hypercholesterolemia, or diabetes. The pressures were included in the regressions one at a time. The solid squares are centered on the point estimate, and the horizontal lines extending from squares represent 95% CIs.
Figure S9. Odds ratios (ORs) and 95% confidence intervals (CIs) for the risk of silent cerebrovascular lesions per 1-SD increase in systolic blood pressure (SBP) when one of the ambulatory blood pressure, home blood pressure, or casual/clinic blood pressure values are included in the same multiple logistic regression model for subjects with no antihypertensive medications. Adjusted for age, sex, body mass index, smoking status, drinking status, and history of cardiovascular diseases, atrial fibrillation, hypercholesterolemia, or diabetes. The solid squares are centered on the point estimate, and the horizontal lines extending from squares represent 95% CIs.
Figure S10. Odds ratios (ORs) and 95% confidence intervals (CIs) for the risk of silent cerebrovascular lesions per 1-SD increase in systolic blood pressure (SBP) for subjects with antihypertensive medications. Adjusted for age, sex, body mass index, smoking status, drinking status, and history of cardiovascular diseases, atrial fibrillation, hypercholesterolemia, or diabetes. The pressures were included in the regressions one at a time. The solid squares are centered on the point estimate, and the horizontal lines extending from squares represent 95% CIs.
Figure S11. Odds ratios (ORs) and 95% confidence intervals (CIs) for the risk of silent cerebrovascular lesions per 1-SD increase in systolic blood pressure (SBP) when one of the ambulatory blood pressure, home blood pressure, or casual/clinic blood pressure values are included in the same multiple logistic regression model for subjects with antihypertensive medications Adjusted for age, sex, body mass index, smoking status, drinking status, and history of cardiovascular diseases, atrial fibrillation, hypercholesterolemia, or diabetes. The solid squares are centered on the point estimate, and the horizontal lines extending from squares represent 95% CIs.
Figure S12. Odds ratios (ORs) and 95% confidence intervals (CIs) for the risk of carotid atherosclerosis per 1-SD increase in systolic blood pressure (SBP) for subjects with no antihypertensive medications. Adjusted for age, sex, body mass index, smoking status, drinking status, and history of cardiovascular diseases, hypercholesterolemia, or diabetes. The pressures were included in the regressions one at a time. The solid squares are centered on the point estimate, and the horizontal lines extending from squares represent 95%CIs.
Figure S13. Odds ratios (ORs) and 95% confidence intervals (CIs) for the risk of carotid atherosclerosis per 1-SD increase in systolic blood pressure (SBP) when one of the ambulatory blood pressure and home blood pressure values are included in the same multiple logistic regression model for subjects with no antihypertensive medications adjusted for age, sex, body mass index, smoking status, drinking status, and history of cardiovascular diseases, hypercholesterolemia, or diabetes. The solid squares are centered on the point estimate, and the horizontal lines extending from squares represent 95% CIs.
SBP per 1-SD increase

Ambulatory
24-h

Ambulatory
Daytime

Ambulatory
Nighttime

Home

Casual/Clinic

OR and 95%CI

Percentage increase in risk (95% CI)

50% (10% to 104%)

41% (4% to 92%)

52% (11% to 108%)

73% (23% to 144%)

34% (-2% to 82%)

Figure S14. Odds ratios (ORs) and 95% confidence intervals (CIs) for the risk of carotid atherosclerosis per 1-SD increase in systolic blood pressure (SBP) for subjects with antihypertensive medications. Adjusted for age, sex, body mass index, smoking status, drinking status, and history of cardiovascular diseases, hypercholesterolemia, or diabetes. The pressures were included in the regressions one at a time. The solid squares are centered on the point estimate, and the horizontal lines extending from squares represent 95%CIs.
Figure S15. Odds ratios (ORs) and 95% confidence intervals (CIs) for the risk of carotid atherosclerosis per 1-SD increase in systolic blood pressure (SBP) when one of the ambulatory blood pressure and home blood pressure values are included in the same multiple logistic regression model for subjects with antihypertensive medications. Adjusted for age, sex, body mass index, smoking status, drinking status, and history of cardiovascular diseases, hypercholesterolemia, or diabetes. The solid squares are centered on the point estimate, and the horizontal lines extending from squares represent 95% CIs.
Figure S16. Odds ratios (ORs) and 95% confidence intervals (CIs) for the risk of silent cerebrovascular lesions per 1-SD increase in daytime and nighttime systolic blood pressure (SBP) variability, nocturnal decline, and morning pressor surge

Adjusted for age, sex, body mass index, smoking status, drinking status, antihypertensive medication, and history of cardiovascular diseases, atrial fibrillation, hypercholesterolemia, or diabetes. The parameters were included in the regressions one at a time. The solid squares are centered on the point estimate, and the horizontal lines extending from squares represent 95% CIs.
**Ambulatory monitoring parameters of SBP per 1-SD increase**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>OR and 95% CI</th>
<th>Percentage increase in risk (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>Ambulatory variability Daytime</td>
<td></td>
<td>15% (-5% to 40%)</td>
</tr>
<tr>
<td>Ambulatory variability Nighttime</td>
<td></td>
<td>24% (2% to 50%)</td>
</tr>
<tr>
<td>Nocturnal decline</td>
<td></td>
<td>-4% (-20% to 16%)</td>
</tr>
<tr>
<td>Morning pressor surge</td>
<td></td>
<td>5% (-13% to 27%)</td>
</tr>
</tbody>
</table>

**Figure S17. Odds ratios (ORs) and 95% confidence intervals (CIs) for the risk of carotid atherosclerosis per 1-SD increase in daytime and nighttime systolic blood pressure (SBP) variability, nocturnal decline, and morning pressor surge**

Adjusted for age, sex, body mass index, smoking status, drinking status, antihypertensive medication, and history of cardiovascular diseases, hypercholesterolemia, or diabetes. The parameters were included in the regressions one at a time. The solid squares are centered on the point estimate, and the horizontal lines extending from squares represent 95%CIs.
Figure S18. Odds ratios (ORs) and 95% confidence intervals (CIs) for the risk of carotid atherosclerosis per 1-SD increase in daytime and nighttime systolic blood pressure (SBP) variability, nocturnal decline, and morning pressor surge when one corresponding SBP values are simultaneously included in the multiple logistic regression model

Adjusted for age, sex, body mass index, smoking status, drinking status, antihypertensive medication, and history of cardiovascular diseases, hypercholesterolemia, or diabetes. The solid squares are centered on the point estimate, and the horizontal lines extending from squares represent 95%CIs.
Figure S19. Odds ratios (ORs) and 95% confidence intervals (CIs) for the risk of silent cerebrovascular lesions per 1-SD increase in heart rate (HR) for subjects without history of cardiovascular diseases. Adjusted for age, sex, body mass index, smoking status, drinking status, antihypertensive medication, and history of cardiovascular diseases, atrial fibrillation, hypercholesterolemia, or diabetes. The HRs were included in the regressions one at a time. The solid squares are centered on the point estimate, and the horizontal lines extending from squares represent 95%CIs.
Figure S20. Odds ratios (ORs) and 95% confidence intervals (CIs) for the risk of carotid atherosclerosis per 1-SD increase in heart rate (HR) for subjects without history of cardiovascular diseases

Adjusted for age, sex, body mass index, smoking status, drinking status, antihypertensive medication, and history of cardiovascular diseases, hypercholesterolemia, or diabetes. The HRs were included in the regressions one at a time. The solid squares are centered on the point estimate, and the horizontal lines extending from squares represent 95%CIs.
Figure S21. Odds ratios (ORs) and 95% confidence intervals (CIs) for the risk of silent cerebrovascular lesions per 1-SD increase in systolic blood pressure (SBP) when home blood pressure values averaged over 7 days of measurements (with the exception of the first day) in accordance with a guideline of the European Society of Hypertension (ESH) and one of the ambulatory blood pressure or casual/clinik blood pressure values were included in the same multiple logistic regression model. Adjusted for age, sex, body mass index, smoking status, drinking status, antihypertensive medication, and history of cardiovascular diseases, atrial fibrillation, hypercholesterolemia, or diabetes. The solid squares are centered on the point estimate, and the horizontal lines extending from squares represent 95% CIs.
Figure S22. Odds ratios (ORs) and 95% confidence intervals (CIs) for the risk of carotid atherosclerosis per 1-SD increase in systolic blood pressure (SBP) when home blood pressure values averaged over 7 days of measurements (with the exception of the first day) in accordance with a guideline of the European Society of Hypertension (ESH) and one of the ambulatory blood pressure or casual/clinic blood pressure values were included in the same multiple logistic regression model. Adjusted for age, sex, body mass index, smoking status, drinking status, antihypertensive medication, and history of cardiovascular diseases, hypercholesterolemia, or diabetes. The solid squares are centered on the point estimate, and the horizontal lines extending from squares represent 95% CIs.