White-Coat and Masked Hypertension Are Associated With Carotid Atherosclerosis in a General Population

The Hisayama Study

Masayo Fukuhara, MD, PhD; Hisatomi Arima, MD, PhD; Toshiharu Ninomiya, MD, PhD; Jun Hata, MD, PhD; Yoichiro Hirakawa, MD, PhD; Yasufumi Doi, MD, PhD; Koji Yonemoto, PhD; Naoko Mukai, MD, PhD; Masaharu Nagata, MD, PhD; Fumie Ikeda, MD, PhD; Kiyoshi Matsumura, MD, PhD; Takanari Kitazono, MD, PhD; Yutaka Kiyohara, MD, PhD

Background and Purpose—On the basis of combined measurements of clinic blood pressure (CBP) and home blood pressure (HBP), blood pressure status can be divided into normotension, white-coat hypertension (WCHT), masked hypertension (MHT), and sustained hypertension (SHT). Despite the clear impact of MHT and SHT on clinical and subclinical arterial disease, uncertainty about the influence of WCHT remains. The objective of this study was to investigate the associations of WCHT, MHT, and SHT with carotid atherosclerosis in a general population.

Methods—This is a cross-sectional survey of 2915 community-dwelling Japanese aged ≥40 years. Normotension was defined as CBP<140/90 and HBP<135/85 mm Hg; WCHT, CBP≥140/90 and HBP<135/85 mm Hg; MHT, CBP<140/90 and HBP≥135/85 mm Hg; and SHT, CBP≥140/90 and HBP≥135/85 mm Hg. Mean intima-media thickness of carotid arteries was measured using a computer-automated system, and carotid stenosis was defined as diameter stenosis ≥30%.

Results—There were 1374 subjects (47.1%) with normotension, 200 (6.9%) with WCHT, 639 (21.9%) with MHT, and 702 (24.1%) with SHT. The geometric average of mean intima-media thickness was significantly higher among subjects with WCHT (0.73 mm), MHT (0.77 mm), and SHT (0.77 mm) than those with normotension (0.67 mm; all P<0.001 versus normotension). Compared with normotension, all types of hypertension were also associated with increased likelihood of carotid stenosis (age- and sex-adjusted odds ratio, 2.36 [95% confidence interval, 1.27–4.37] for WCHT, 1.95 [1.25–3.03] for MHT, and 3.02 [2.01–4.54] for SHT). These associations remained significant even after adjustment for other cardiovascular risk factors.

Conclusions—WCHT, as well as MHT, and SHT were associated with carotid atherosclerosis in a general Japanese population. (Stroke. 2013;44:1512-1517.)

Key Words: atherosclerosis ■ clinic blood pressure ■ home blood pressure ■ intima-media thickness ■ masked hypertension ■ white-coat hypertension

On the basis of combined measurements of clinic blood pressure (CBP) and out-of-office blood pressure (BP), such as home blood pressure (HBP) and ambulatory BP, BP status can be divided into 4 categories: normotension (NT), white-coat hypertension (WCHT), masked hypertension (MHT), and sustained hypertension (SHT).1,2 Although several authors have reported clear associations of MHT and SHT with cardiovascular disease,3-7 there is still uncertainty about the influence of WCHT on subclinical organ damage, such as carotid atherosclerosis.4,5,7-9 As well as on cardiovascular or renal disease.3,6,10-13

Present guidelines for the management of hypertension recommend assessment of subclinical arterial disease as an intermediate stage in the continuum of vascular disease among subjects at high risk of cardiovascular disease.1,14 Among several noninvasive screening tests of subclinical arterial disease, ultrasound examination of the carotid arteries with assessment of intima-media thickness (IMT) and atherosclerotic plaques has been clearly shown to be useful in predicting the future risks of coronary heart disease and stroke.15-17

In the present cross-sectional study, we evaluated the associations of WCHT, MHT, and SHT defined using CBP and HBP with carotid atherosclerosis evaluated using ultrasound examination in a general Japanese population.

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1512
Methods

Study Population
The Hisayama study is a population-based prospective cohort study of cardiovascular disease established in 1961 in the town of Hisayama, a suburb of the Fukuoka metropolitan area on Kyushu Island, Japan.14,15 On the basis of data from the national census, the age and occupational distributions in Hisayama have been almost identical to those in Japan since the 1960s.14,15 The present cross-sectional study was based on a screening survey conducted in 2007 and 2008. A total of 3376 residents aged ≥20 years (78.0% of the total population of this age group) consented to participate in the examination and underwent a comprehensive assessment, including HBP measurement and carotid ultrasonography. After the exclusion of 211 subjects without HBP measurements for >3 days, 75 subjects without information on carotid ultrasonography. After the exclusion of 211 subjects without information on carotid ultrasonography and 175 subjects lacking both types of information, a total of 2915 subjects (1267 men and 1648 women) were enrolled in the present study.

CBP Measurements
CBP was measured 3 times using an automated sphygmomanometer (BP-203 RVIIIIB; Omron Healthcare Co, Ltd, Kyoto, Japan) based on the cuff oscillometric method with an appropriately sized cuff on the right arm in the sitting position after rest for ≥5 minutes. The mean of the 3 measurements was used for the analysis.

HBP Measurements
Before starting the HBP measurements, physicians and public health nurses taught the subjects how to measure their HBP accurately. The subjects were advised to measure their HBP 3 times: every morning before breakfast, within 1 hour of waking, and after >5 minutes of rest in the sitting position for 4 weeks. Participants on BP-lowering medication were advised to measure their HBP before taking medication. The subjects were also instructed to place appropriately sized cuffs directly around their nondominant arms and to maintain the position of the cuffs at the level of the heart. HBP measurements were performed using an automatic device (HEM-7080IC; Omron Healthcare Co, Ltd) based on the cuff oscillometric method. HEM-7080IC uses the identical components and BP determining algorithm as another device, HEM-705IT, which was previously validated and satisfied the criteria of the British Hypertension Society protocol.23 The device has a memory, which allows recording of 350 measurements, and a data output port, which enables data extraction for the analysis. The mean value of all available daily averages was used in the present analysis.

BP Classification
On the basis of the combined measurements of CBP and HBP, irrespective of the use of antihypertensive medication, the subjects were divided into 4 groups: NT (CBP <140/90 mm Hg and HBP <135/85 mm Hg), WCHT (CBP ≥140/90 mm Hg and HBP <135/85 mm Hg), MHT (CBP <140/90 mm Hg and HBP ≥135/85 mm Hg), and SHT (CBP ≥140/90 mm Hg and HBP ≥135/85 mm Hg).1,2,14

Carotid Ultrasoundography
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. The ultrasound examination was performed in a supine position by specially trained laboratory technicians using a standardized technique. The technicians were blinded to the medical history, BP values, and laboratory data of each participant. Mean IMT was measured using the long-axis view of each common carotid artery. An image was obtained in the region 20 mm proximal to the origin of the bulb at the far wall of each common carotid artery, and the average IMT as a mean value of IMT measurements at 250 computer-based points in the region was automatically calculated on each side using a computer-assisted measurement system (Intimascope; Media Cross Co, Ltd, Tokyo, Japan).23 Mean IMT was defined as the mean of the left and right sides of the average IMT. Maximum IMT in the possible areas of observation of the left and right common carotid arteries, bulbs, and internal carotid arteries was measured manually using the short-axis view, and carotid wall thickening was defined as a maximum IMT of ≥1.0 mm. Percent diameter stenosis was measured on the short-axis view using the European Carotid Surgery Trial method,24 and carotid stenosis was defined as a percent diameter stenosis of ≥30%.

Other Risk Factor Measurements
Details about other risk factor measurements are in the online-only Data Supplement.

Statistical Analysis
The differences in the mean values or frequencies of risk factors across BP categories were tested using an ANOVA or a logistic regression model. IMT was log-transformed to remove skewness, and geometric means were reported by back transformation. The effects of BP categories on the adjusted average of the mean and maximum IMT were assessed using an ANCOVA. The age- and sex-adjusted prevalence rate of carotid wall thickening and carotid stenosis were calculated using the direct method. The age- and sex-adjusted or multivariable-adjusted odds ratio and its 95% confidence interval (CI) for the presence of carotid wall thickening or carotid stenosis were assessed using a multivariable logistic regression model. The heterogeneity in the effects of BP categories on outcomes between subgroups was estimated by adding interaction terms to the relevant statistical model. All statistical analyses were performed using the SAS program package version 9.3 (SAS Institute, Inc, Cary, NC). P values of <0.05 were considered statistically significant.

Ethical Considerations
The study protocol was approved by Kyushu University Institutional Review Board for Clinical Research, and the procedures followed were in accordance with national guidelines. All participants provided written informed consent.

Results
Baseline characteristics of included (n=2915) and excluded participants (n=461) in the study are shown in Table I in the online-only Data Supplement. Compared with the included subjects, those excluded were significantly older and had higher levels of CBP. Use of antihypertensive medication and history of cardiovascular disease were more prevalent in excluded participants.

Among the 2915 subjects included, there were 1374 (47.1%) with NT, 200 (6.9%) with WCHT, 639 (21.9%) with MHT, and 702 (24.1%) with SHT. The mean values or frequencies of cardiovascular risk factors are listed, according to BP categories in Table 1. Compared with the NT group, subjects with WCHT, MHT, and SHT were significantly older and had higher CBP and HBP levels. The subjects with WCHT, MHT, and SHT were more likely to have diabetes mellitus and to receive antihypertensive and lipid-lowering medication compared with the NT subjects.

Among the total subjects, the geometric average of mean IMT was 0.72 mm (95% CI, 0.71–0.72). The crude geometric average of the mean IMT was significantly higher in the WCHT (0.73 mm; 95% CI, 0.71–0.75), MHT (0.77 mm; 0.76–0.78), and SHT (0.77 mm; 0.76–0.78) groups than the NT group (0.67 mm; 0.66–0.68; all P<0.001 versus NT). These associations remained significant even after adjustment for other cardiovascular risk factors, such as age, sex, diabetes,...
Among the total subjects, the geometric average of the maximum IMT was 1.21 mm (95% CI, 1.19–1.23). Compared with the NT group (1.07 mm; 95% CI, 1.04–1.09), the WCHT (1.31 mm; 1.24–1.38), MHT (1.36 mm; 1.32–1.40), and SHT (1.36 mm; 1.33–1.41) groups had clearly higher values of the maximum IMT (all $P<0.001$ versus NT). These associations remained significant even after adjusting for other cardiovascular risk factors (NT 1.15 mm [95% CI, 1.13–1.17], WCHT 1.30 mm [1.24–1.37], MHT 1.24 mm [1.21–1.28], and SHT 1.27 mm [1.24–1.31]; all $P<0.001$ versus NT; Figure 2). There were no clear differences in maximum IMT

**Table 1. Baseline Characteristics of Participants, According to Blood Pressure Category**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Normotension (n=1374)</th>
<th>White-Coat HT (n=200)</th>
<th>Masked HT (n=639)</th>
<th>Sustained HT (n=702)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>58.7±11.3</td>
<td>64.0±10.1†</td>
<td>67.2±11.1†</td>
<td>66.1±11.4†</td>
</tr>
<tr>
<td>Men, %</td>
<td>36.9</td>
<td>39.0</td>
<td>49.6†</td>
<td>52.0†</td>
</tr>
<tr>
<td>Clinic systolic blood pressure, mmHg</td>
<td>118.4±11.7</td>
<td>150.0±9.0†</td>
<td>128.4±8.8†</td>
<td>154.2±11.9†</td>
</tr>
<tr>
<td>Clinic diastolic blood pressure, mmHg</td>
<td>73.1±7.7</td>
<td>88.6±7.2†</td>
<td>77.7±7.2†</td>
<td>90.3±8.5†</td>
</tr>
<tr>
<td>Home systolic blood pressure, mmHg</td>
<td>117.6±10.1</td>
<td>126.3±6.5†</td>
<td>144.9±11.0†</td>
<td>151.0±13.1†</td>
</tr>
<tr>
<td>Home diastolic blood pressure, mmHg</td>
<td>71.6±6.9</td>
<td>74.8±6.7†</td>
<td>83.0±8.3†</td>
<td>85.2±9.7†</td>
</tr>
<tr>
<td>Days of home blood measurement</td>
<td>25.0±6.2</td>
<td>26.2±5.0*</td>
<td>25.5±6.0</td>
<td>24.7±6.8</td>
</tr>
<tr>
<td>Antihypertensive medication, %</td>
<td>13.5</td>
<td>34.0†</td>
<td>49.9†</td>
<td>48.3†</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>9.2</td>
<td>26.0†</td>
<td>22.2</td>
<td>24.5†</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>5.45±0.93</td>
<td>5.60±0.98</td>
<td>5.29±0.91†</td>
<td>5.46±0.85</td>
</tr>
<tr>
<td>HDL-cholesterol, mmol/L</td>
<td>1.80±0.46</td>
<td>1.72±0.47</td>
<td>1.68±0.43†</td>
<td>1.66±0.46†</td>
</tr>
<tr>
<td>Lipid-lowering medication, %</td>
<td>10.4</td>
<td>21.0†</td>
<td>19.4†</td>
<td>20.7†</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>22.2±3.0</td>
<td>24.1±4.1†</td>
<td>23.5±3.2†</td>
<td>23.4±3.7†</td>
</tr>
<tr>
<td>Current drinking, %</td>
<td>47.3</td>
<td>40.0</td>
<td>52.3*</td>
<td>52.6*</td>
</tr>
<tr>
<td>Current smoking, %</td>
<td>19.4</td>
<td>8.0†</td>
<td>20.5</td>
<td>20.2</td>
</tr>
<tr>
<td>Regular exercise, %</td>
<td>11.4</td>
<td>11.0</td>
<td>12.7</td>
<td>14.8*</td>
</tr>
<tr>
<td>History of cardiovascular disease, %</td>
<td>3.2</td>
<td>5.0</td>
<td>8.0†</td>
<td>6.7†</td>
</tr>
</tbody>
</table>

All values are given as the means±SD or as a percentage. HDL indicates high-density lipoprotein; and HT, hypertension.

* $P<0.05$.

† $P<0.001$ vs normotension.

mellitus, total cholesterol, high-density lipoprotein–cholesterol, body mass index, smoking, drinking, exercise, antihypertensive medication, and lipid-lowering medication, and lipid-lowering medication (NT 0.70 mm [95% CI, 0.69–0.70]; WCHT 0.72 mm [0.70–0.73]; MHT 0.74 mm [0.73–0.75]; and SHT 0.74 mm [0.73–0.75]; all $P<0.001$ versus NT; Figure 1). The difference between WCHT and SHT reached statistical significance ($P=0.03$), whereas there were no significant differences between WCHT and MHT ($P=0.055$) or MHT and SHT ($P=0.98$). Similar results were obtained from multivariable analysis with a past history of cardiovascular disease (data not shown).
There were similar associations of WCHT, MHT, and SHT with mean IMT (P heterogeneity=0.14), maximum IMT (P heterogeneity=0.59), carotid wall thickening (P heterogeneity=0.33), and carotid stenosis (P heterogeneity=0.92) between the participant subgroups defined by the use of antihypertensive medication, although the effects of WCHT did not reach statistical significance among subjects with antihypertensive medication, probably because of the limited number of subjects (Tables II and III in the online-only Data Supplement).

**Discussion**

The findings from the present population-based cross-sectional study provided good evidence of clear associations of all types of hypertension, including WCHT, defined using CBP and HBP with increased risks of carotid wall thickening and carotid stenosis. These associations remained significant even after adjustment for potential confounding factors, such as age, sex, diabetes mellitus, total cholesterol, high-density lipoprotein–cholesterol, body mass index, smoking, drinking, exercise, antihypertensive medication, and lipid-lowering medication.

Although several studies have reported positive associations between WCHT and carotid atherosclerosis,4,9,25 present evidence is mainly derived from hospital-based case-control or case-series studies. Furthermore, most previous studies defined WCHT using ambulatory BP, but HBP measurement is more widely available and better accepted. A population-based study of 812 individuals from a general Japanese population investigated the association of WCHT defined using HBP with carotid atherosclerosis, but it failed to demonstrate a clear influence of WCHT on carotid wall thickening.4 In the present large-scale population-based study, however, WCHT as well as MHT and SHT defined using HBP were clearly associated with carotid wall thickening and carotid stenosis. With regard to clinical cardiovascular events, most of the previous prospective studies failed to demonstrate clear influence of WCHT on cardiovascular disease, probably because of the relative small number of subjects with WCHT. However, a meta-analysis of prospective cohort studies demonstrated a nonsignificant trend toward increased risk of stroke incidence among subjects with WCHT.12 On the basis of the totality of the present evidence, there seems to be a link between WCHT and clinical/subclinical cardiovascular disease, but larger studies with longer periods of follow-up are necessary to clarify this issue. Meanwhile, as recommended by the present guidelines for management of hypertension,1,14 routine use of antihypertensive medication for subjects with WCHT should be avoided, particularly for those without organ damage or cardiovascular disease.

The mechanisms underlying the association between WCHT and carotid atherosclerosis have not been completely resolved. One possible mechanism is that increased sympathetic tone, which is commonly observed in subjects with WCHT,26 may promote the development and progression of arterial damage. Another possible mechanism involves insulin resistance, which is associated with WCHT as well as a risk of atherosclerosis.26 It is also possible that a decrease in baroreflex sensitivity associated with carotid atherosclerosis27,28 increases BP variability, which is frequently observed in WCHT.

In the present analysis, MHT and SHT were also clearly associated with increased risks of carotid wall thickening and carotid stenosis. These findings are directly in line with the results of previous observational studies that identified close associations of MHT and SHT with carotid atherosclerosis,4,5,7 other forms of subclinical arterial disease,7 and cardiovascular disease.6,7

Several cross-sectional studies have reported that carotid IMT was significantly thinner in WCHT than in MHT or SHT.4,9,25 These discrepant findings are likely attributable to the differences in the definition of WCHT and the selection of the study population. For example, studies using CBP defined WCHT by a higher threshold than those using HBP, and in previous studies most of the subjects with WCHT were younger than those with MHT or SHT. Conversely, in the present study, WCHT was defined as a difference of 30% between CBP and HBP without any restriction of age. Further prospective studies are necessary to clarify this issue.

**Table 2. Age- and Sex-Adjusted Prevalence and Adjusted OR of Carotid Wall Thickening and Carotid Stenosis, According to Blood Pressure Category**

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Normotension (n=1374)</th>
<th>White-Coat HT (n=200)</th>
<th>Masked HT (n=639)</th>
<th>Sustained HT (n=702)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Carotid wall thickening</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>603</td>
<td>134</td>
<td>438</td>
<td>476</td>
</tr>
<tr>
<td>Age- and sex-adjusted prevalence, %</td>
<td>51.3</td>
<td>65.6</td>
<td>60.8</td>
<td>60.8</td>
</tr>
<tr>
<td>Age- and sex-adjusted OR (95% Cl)</td>
<td>1.00 (reference)</td>
<td>2.00 (1.43–2.81)</td>
<td>1.58 (1.27–1.97)</td>
<td>1.60 (1.30–1.98)</td>
</tr>
<tr>
<td>Multivariable-adjusted OR (95% Cl)†</td>
<td>1.00 (reference)</td>
<td>1.86 (1.32–2.64)</td>
<td>1.49 (1.18–1.88)</td>
<td>1.48 (1.18–1.85)</td>
</tr>
<tr>
<td><strong>Carotid stenosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>38</td>
<td>16</td>
<td>55</td>
<td>84</td>
</tr>
<tr>
<td>Age- and sex-adjusted prevalence, %</td>
<td>3.8</td>
<td>7.4</td>
<td>6.8</td>
<td>10.1</td>
</tr>
<tr>
<td>Age- and sex-adjusted OR (95% Cl)</td>
<td>1.00 (reference)</td>
<td>2.36 (1.27–4.37)</td>
<td>1.95 (1.25–3.03)</td>
<td>3.02 (2.01–4.54)</td>
</tr>
<tr>
<td>Multivariable-adjusted OR (95% Cl)†</td>
<td>1.00 (reference)</td>
<td>2.45 (1.30–4.62)</td>
<td>1.95 (1.23–3.08)</td>
<td>3.03 (1.97–4.67)</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; HT, hypertension; and OR, odds ratio.  
*Maximum intima-media thickness >1.0 mm.  
†Adjusted for age, sex, diabetes mellitus, total cholesterol, high-density lipoprotein–cholesterol, body mass index, smoking, drinking, exercise, antihypertensive medication and lipid-lowering medication.  
‡Percent diameter stenosis ≥30%.
SHT, whereas other studies showed no significant differences. In the present study, mean IMT was significantly lower among subjects with WCHT than among those with SHT, although there were no significant differences in maximum IMT across the 3 types of hypertension. Future large studies will be needed to clarify whether the risk of carotid atherosclerosis is modest in WCHT compared with that in MHT and SHT.

To our knowledge, this is the largest population-based study to demonstrate the close association between WCHT and carotid atherosclerosis, although corresponding definitive evidence about the influence of WCHT in each subgroup defined by the use of antihypertensive medication was not provided in the present analysis. The present study has several limitations. First, because of the cross-sectional nature of this study, we were unable to determine whether there is a causal relationship between WCHT and carotid atherosclerosis. Second, several laboratory technicians measured maximum IMT and carotid stenosis manually without assessment of inter-rater reliability, although they were specially trained to use a standardized technique. This limitation, however, is not likely to invalidate the findings observed in the present analysis because similar results were obtained for mean IMT, which was estimated automatically using a computer-assisted measurement system. Third, compared with the subjects included in the study, those excluded were older and had higher levels of CBP and more frequent history of cardiovascular disease. Therefore, our findings may not be applicable to old or high-risk populations. Fourth, inclusion of participants on antihypertensive medication may have resulted in misclassification of BP categories. However, stratified analysis demonstrated comparable influence of each type of hypertension on carotid atherosclerosis between participants with and without antihypertensive medication. Fifth, CBP was classified based on just 3 measurements on a single day in the present study. However, this source of variability could not account for the relation observed in the present study because a random misclassification of this nature would tend to cause an underestimation of the study findings. Sixth, possible confounding of unknown risk factors may not be fully adjusted for, although we included all the traditional risk factors for cardiovascular disease in statistical models.

Conclusions
WCHT as well as MHT and SHT were associated with carotid atherosclerosis in a general Japanese population. Because WCHT is not likely to be totally benign, subjects with WCHT seem to require lifestyle changes and a close follow-up as recommended by present guidelines for the management of hypertension.

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Disclosures
None.

References


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http://stroke.ahajournals.org/content/suppl/2013/05/03/STROKEAHA.111.000704.DC1

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Supplemental Methods

Other Risk Factor Measurements
Each participant completed a self-administered questionnaire covering medical history, including treatment for hypertension, diabetes mellitus, and hyperlipidemia, smoking habits, alcohol intake, and regular exercise. Smoking habits and alcohol intake were classified into currently habitual or not. The subjects engaging in sports or other forms of exertion ≥3 times a week during their leisure time made up a regular exercise group. Body height and weight were measured in light clothing without shoes, and the body mass index (kg/m²) was calculated. Serum total and high-density lipoprotein (HDL) cholesterol levels were determined enzymatically. Blood glucose levels were measured by the hexokinase method. Diabetes mellitus was determined by medical history, plasma glucose levels (fasting glucose level ≥7.0 mmol/L or postprandial glucose level ≥11.1 mmol/L), or a 75-g oral glucose tolerance test using the 1998 World Health Organization criteria.⁴ History of cardiovascular disease was defined as any preexisting events of stroke or coronary heart disease, including myocardial infarction and coronary intervention. All cardiovascular events were adjudicated on the basis of physical examinations and a review of all available clinical information including medical records and imaging.
**Table I. Baseline Characteristics of Included and Excluded Participants in the Study**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Included participants (n=2,915)</th>
<th>Excluded participants (n=461)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>62.7 ± 11.8</td>
<td>71.6 ± 15.6†</td>
</tr>
<tr>
<td>Male, %</td>
<td>43.5</td>
<td>41.4</td>
</tr>
<tr>
<td>Clinic systolic blood pressure, mmHg</td>
<td>131.4 ± 18.8</td>
<td>136.0 ± 22.6†</td>
</tr>
<tr>
<td>Clinic diastolic blood pressure, mmHg</td>
<td>79.3 ± 10.7</td>
<td>78.4 ± 12.7</td>
</tr>
<tr>
<td>Antihypertensive medication, %</td>
<td>31.3</td>
<td>37.3*</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>16.9</td>
<td>14.1</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>5.43 ± 0.91</td>
<td>5.13 ± 1.11†</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>1.73 ± 0.46</td>
<td>1.63 ± 0.49†</td>
</tr>
<tr>
<td>Lipid-lowering medication, %</td>
<td>15.6</td>
<td>13.9</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>23.1 ± 3.4</td>
<td>21.9 ± 3.7†</td>
</tr>
<tr>
<td>Current drinking, %</td>
<td>49.2</td>
<td>31.8†</td>
</tr>
<tr>
<td>Current smoking, %</td>
<td>19.1</td>
<td>22.2</td>
</tr>
<tr>
<td>Regular exercise, %</td>
<td>12.5</td>
<td>5.0</td>
</tr>
<tr>
<td>History of cardiovascular disease, %</td>
<td>5.2</td>
<td>14.8†</td>
</tr>
</tbody>
</table>

Abbreviations: HT, hypertension; HDL, high density lipoprotein.
All values are given as the means ± SD or as a percentage.
*p<0.05, †p<0.001.
### Supplemental Table II. Multivariable-adjusted Geometric Average of Mean and Maximum Intima-media Thickness According to Blood Pressure Category among Participants without and with Antihypertensive Medication

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Normotension</th>
<th>White-coat HT</th>
<th>Masked HT</th>
<th>Sustained HT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean intima-media thickness</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No antihypertensive medication</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of participants</td>
<td>1,189</td>
<td>132</td>
<td>320</td>
<td>363</td>
</tr>
<tr>
<td>Geometric average (95%CI)*</td>
<td>0.69 (0.69-0.70)</td>
<td>0.73 (0.71-0.75)†</td>
<td>0.73 (0.72-0.75)‡</td>
<td>0.74 (0.73-0.75)‡</td>
</tr>
<tr>
<td>Antihypertensive medication</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of participants</td>
<td>185</td>
<td>68</td>
<td>319</td>
<td>339</td>
</tr>
<tr>
<td>Geometric average (95%CI)*</td>
<td>0.71 (0.69-0.72)</td>
<td>0.70 (0.68-0.73)</td>
<td>0.75 (0.73-0.76)‡</td>
<td>0.74 (0.73-0.76)‡</td>
</tr>
<tr>
<td>Maximum intima-media thickness</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No antihypertensive medication</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of participants</td>
<td>1,189</td>
<td>132</td>
<td>320</td>
<td>363</td>
</tr>
<tr>
<td>Geometric average (95%CI)*</td>
<td>1.13 (1.11-1.16)</td>
<td>1.32 (1.24-1.40)‡</td>
<td>1.24 (1.19-1.29)‡</td>
<td>1.26 (1.21-1.30)‡</td>
</tr>
<tr>
<td>Antihypertensive medication</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of participants</td>
<td>185</td>
<td>68</td>
<td>319</td>
<td>339</td>
</tr>
<tr>
<td>Geometric average (95%CI)*</td>
<td>1.19 (1.13-1.25)</td>
<td>1.28 (1.18-1.39)**</td>
<td>1.27 (1.23-1.33)‡</td>
<td>1.30 (1.26-1.36)‡</td>
</tr>
</tbody>
</table>

Abbreviations: HT, hypertension; CI, confidence interval.

*Adjusted for age, sex, diabetes mellitus, total cholesterol, high-density lipoprotein cholesterol, body mass index, smoking, drinking, exercise, and lipid-lowering medication.

**p<0.05, †p<0.01, ‡p<0.001 vs normotension without antihypertensive medication.
### Supplemental Table III. Age- and Sex-adjusted Prevalence and Adjusted Odds Ratio of Carotid Wall Thickening and Carotid Stenosis According to Blood Pressure Category among Participants without and with Antihypertensive Medication

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Normotension</th>
<th>White-coat HT</th>
<th>Masked HT</th>
<th>Sustained HT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carotid wall thickening*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No antihypertensive medication</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases / participants</td>
<td>487 / 1,189</td>
<td>86 / 132</td>
<td>210 / 320</td>
<td>222 / 363</td>
</tr>
<tr>
<td>Age- and sex-adjusted prevalence, %</td>
<td>49.8</td>
<td>66.1</td>
<td>62.4</td>
<td>58.2</td>
</tr>
<tr>
<td>Multivariable-adjusted odds ratio (95% CI)**</td>
<td>1.00 (reference)</td>
<td>2.08 (1.38-3.15)</td>
<td>1.66 (1.24-2.21)</td>
<td>1.42 (1.08-1.86)</td>
</tr>
<tr>
<td>Antihypertensive medication</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases / participants</td>
<td>116 / 185</td>
<td>48 / 68</td>
<td>228 / 319</td>
<td>254 / 339</td>
</tr>
<tr>
<td>Age- and sex-adjusted prevalence, %</td>
<td>58.9</td>
<td>63.0</td>
<td>57.9</td>
<td>63.1</td>
</tr>
<tr>
<td>Multivariable-adjusted odds ratio (95% CI)**</td>
<td>1.00 (reference)</td>
<td>1.33 (0.69-2.57)</td>
<td>1.24 (0.81-1.89)</td>
<td>1.51 (0.98-2.32)</td>
</tr>
<tr>
<td>Carotid stenosis†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No antihypertensive medication</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases / participants</td>
<td>30 / 1,189</td>
<td>9 / 132</td>
<td>22 / 320</td>
<td>33 / 363</td>
</tr>
<tr>
<td>Age- and sex-adjusted prevalence, %</td>
<td>3.7</td>
<td>7.2</td>
<td>5.8</td>
<td>8.5</td>
</tr>
<tr>
<td>Multivariable-adjusted odds ratio (95% CI)**</td>
<td>1.00 (reference)</td>
<td>2.61 (1.16-5.86)</td>
<td>1.71 (0.93-3.12)</td>
<td>2.64 (1.52-4.59)</td>
</tr>
<tr>
<td>Antihypertensive medication</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases / participants</td>
<td>8 / 185</td>
<td>7 / 68</td>
<td>33 / 319</td>
<td>51 / 339</td>
</tr>
<tr>
<td>Age- and sex-adjusted prevalence, %</td>
<td>4.0</td>
<td>7.5</td>
<td>7.6</td>
<td>13.0</td>
</tr>
<tr>
<td>Multivariable-adjusted odds ratio (95% CI)**</td>
<td>1.00 (reference)</td>
<td>2.23 (0.75-6.59)</td>
<td>2.42 (1.07-5.45)</td>
<td>3.80 (1.72-8.38)</td>
</tr>
</tbody>
</table>

Abbreviations: HT, hypertension; CI, confidence interval.
*Maximum intima-media thickness >1.0mm. †Percent diameter stenosis ≥30%.
**Adjusted for age, sex, diabetes mellitus, total cholesterol, high-density lipoprotein cholesterol, body mass index, smoking, drinking, exercise, and lipid-lowering medication.
Supplemental References