Prediction of Stroke by Self-Measurement of Blood Pressure at Home Versus Casual Screening Blood Pressure Measurement in Relation to the Joint National Committee 7 Classification

The Ohasama Study

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Background and Purpose—To compare the predictive power of self-measured home blood pressure (HBP) and casual blood pressure (CBP) for stroke risk in relation to the Joint National Committee 7 (JNC-7) classification.

Methods—HBP and CBP measurements were taken in 1702 subjects (≥40 years) without a history of stroke, who were followed up for an average of 11 years. Subjects were classified into 4 groups on the basis of either HBP or CBP, according to the JNC-7 criteria: group 1 (HBP <115/75 mm Hg; CBP <120/80 mm Hg); group 2 (115/75≤HBP<135/85 mm Hg; 120/80≤CBP<140/90 mm Hg); group 3 (135/85≤HBP<150/95 mm Hg; 140/90≤CBP<160/100 mm Hg); and group 4 (HBP≥150/95 mm Hg; CBP ≥160/100 mm Hg). Groups 2, 3, and 4 were further divided into 2 subgroups (a and b): those without and with cardiovascular disease risks, respectively. The risk of the first stroke in these groups was examined by the Cox hazards model adjusted for age and sex.

Results—The stroke risk in groups 3b and 4b (defined by HBP and CBP) was 2 to 5× higher than that in group 1 with significant differences. The risk in groups 2a, 3a, and even 4a was not significantly different from that in group 1 by the CBP-based classification, but the risk in group 4a was significantly higher than that in group 1 by the HBP-based classification, which also showed a stepwise increase in risk from groups 2a to 4a.

Conclusions—The JNC-7 classification had a stronger predictive power using HBP-based classification compared with CBP-based classification, suggesting the usefulness of HBP in the management of hypertension. (Stroke. 2004;35:2356-2361.)

Key Words: blood pressure ■ hypertension ■ prospective studies ■ stroke

Hypertension is a major risk factor for stroke in developed and developing countries. Accurate diagnosis and treatment of hypertension are necessary for better stroke prevention in the Asia-Pacific region because a high frequency of ischemic and hemorrhagic stroke related to blood pressure (BP) is observed in this region.1

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (Joint National Committee 7 [JNC-7]) is based on recent, up-to-date evidence for handling hypertension.2 The JNC-7 classification has 2 distinctive features compared with past JNC-VI3 and the 1999 World Health Organization—International Society of Hypertension Guidelines:4 risk stratification is simplified to 4 grades on the basis of BP; a new category, 120 to 139 mm Hg systolic BP (SBP) or 80 to 89 mm Hg diastolic BP (DBP), is defined as prehypertension. The JNC-7 recommended that subjects who had a past history of cerebrovascular disease should be treated intensively to prevent the recurrence of stroke. However, there was no specific description of strategies to prevent the first stroke. Although the applicability of JNC-VI was demonstrated in the Japanese population,5 it is still uncertain whether the newer classification could be similarly useful in Asian populations.

We reported that self-measurement of home BP (HBP) was more likely to reflect an individual’s “true” BP and thus has a stronger predictive power for mortality compared with conventional casual BP (CBP).6–8
An objective of this study is to examine whether the JNC-7 classification is applicable in predicting the first-stroke risk among Japanese. Another objective is to compare the predictive power of HBP and CBP for stroke risk in relation to the CBP-based JNC-7 classification.

Methods

Study Population

The present study is part of a longitudinal observational study of subjects who have been participating since 1987 in HBP measurement in Ohasama, which is a rural community in Japan. The socioeconomic and demographic characteristics of this region and the details of the selection of the study subjects have been described previously. Briefly, HBP measured 3× or more and CBP measurements were obtained from 1789 representative individuals of the 1989 eligible individuals aged 40+ years. Eighty-seven individuals had a previous history of stroke, so they were excluded from the present analysis. The study sample consisted of 1702 individuals. The mean (SD) age was 60.6 (10.7) years, and the ratio of men to women was 39:61. The reasons for the disproportionate ratio of men and women were described previously.

The study protocol was approved by the institutional review board of Tohoku University School of Medicine and by the Department of Health of the Ohasama Town Government. Informed consent was obtained from each subject.

BP Measurements

Annual health check-ups are available to all Japanese citizens 40+ years, where CBP is measured. Subjects are seated at rest for 2 minutes, and then CBP is measured by well-trained nurses or technicians. In Ohasama, BPs were measured twice consecutively during the health check-up, using a semiautomatic BP measuring device (HEM401C; Omron Healthcare Co, Ltd) based on the cuff-oscillometric principle, which generates a digital display of systolic and diastolic BP. The devices for measurement of CBP and HBP were calibrated before the start of the study. The mean difference (SD) between HEM401C and USM700F was −0.4 (6.0) mm Hg for SBP and +1.2 (5.8) mm Hg for DBP. All devices met the criteria set by the Association for the Advancement of Medical Instrumentation.

Classification of Groups

According to the JNC-7 criteria, subjects were classified into 4 groups on the basis of either HBP or CBP, as shown in Table 1. When a systolic or diastolic BP was in a different category, the subject was assigned to the higher category. The CBP classification was equal to JNC-7 criteria. In the present analysis, 135/85 mm Hg HBP was defined as hypertension according to the JNC-VI and
Follow-Up and Risk Ascertainment
In the present study, we accumulated follow-up data until December 31, 2001. The incidence and past history of stroke and transient ischemic attack (TIA) were investigated by use of the Stroke Registration System of Iwate Prefecture, death certificates, receipt of National Health Insurance, and questionnaires sent to each household at the time of HBP measurement. This was then confirmed by checking the medical records of Ohasama Hospital, which is the only hospital in the town. Computed tomography (CT) scan and MRI of the brain are available, and >90% of the subjects have their regular check-ups at this facility. We defined stroke and TIA as clinical disorders with focal brain dysfunction. The diagnostic criteria of stroke, TIA, and their subtypes were based on the Classification of Cerebrovascular Disease III by the National Institute of Neurological Disorders and Stroke.12 We used CT scan and MRI to determine the clinical definition of stroke. For 3% of stroke cases, death certificates were the only source of information. The analysis in the present study included only the first event for those who had multiple nonfatal events, whereas subarachnoid hemorrhage (SAH) was excluded as an incident of stroke. Cardiovascular disease risks were the only source of information. The analysis in the present study was based on a comprehensive follow-up system in the study population.

Data Analysis
CBP of each subject was the average of 2 consecutive CBP readings. HBP values were the average of all home measurements per subject.

The risk of first stroke or TIA was examined by using the Cox proportional hazards model. The dependent variable was the number of days from the measurement of the first BP to death or censoring for survivors until December 31, 2001. The independent variables were age, sex, and subgroups of HBP or CBP classifications.

The estimated relative hazard (RH) and the 95% CI of variables were derived from the coefficient and its SE determined by the Cox model. The RH is expressed relative to group 1 (normotensives; RH, 1). All data were expressed as mean (SD) unless otherwise stated. P<0.05 (2-sided test) was considered statistically significant. The SAS system (version 8.02; SAS Institute) was used for all statistical calculations.

Results
Subjects were followed up for a mean of 10.6±3.0 years (maximum of 13.9 years). There were 141 incident cases of first stroke or TIA among the 1702 individuals: 106 (75%) resulting from cerebral infarction, 28 (20%) resulting from intracerebral hemorrhage, 4 (3%) TIA, and 3 (2%) of unknown causes. Twelve events of SAH were observed and excluded from the 141 incident cases.

Characteristics of subjects are shown in Table 2. Of the 1702 study subjects, 370 (22%) were classified as current or ex-smokers; 507 (30%) were treated with antihypertensive medication at baseline; 16 (1%) had a history of heart disease; 218 (13%) of diabetes mellitus; and 207 (12%) of hypercholesterolemia. The mean number of HBP measurements from each individual was 23.0 (7.1). The mean SBP and DBP of all subjects were 125.2 (15.0) and 74.9 (10.1) mm Hg, respectively.

Preliminarily, we analyzed the risk of first onset of stroke or TIA among the 4 groups of BP stratification (Figure 1). The cardiovascular disease risks were used for adjustment of the Cox model instead of risk stratification ("a" and "b"). Linear increases in the risk of stroke or TIA for CBP-based and HBP-based classifications were observed in this sample. The predictive value of HBP was higher than that of CBP; the risk in group 3 was not significantly higher by the CBP-based classification (RH, 1.62; CI, 0.90 to 2.91; P=0.1), but it was significantly higher by the HBP-based classification (RH, 4.07; CI, 1.99 to 8.31; P=0.0001). The statistically significant linearity among the groups was observed for CBP-based (trend P=0.0009) and HBP-based (trend P<0.0001) classifications.

Figure 2 shows the risk of first stroke or TIA of the 7 groups in each CBP-based and HBP-based classification. The RHs in subgroup b, with cardiovascular disease risks on the basis of HBP and CBP, increased linearly with the elevation of BP grade. In group 4b and 4a, the predictability of HBP (4b RH, 6.41; CI, 2.81 to 14.6; P<0.0001; 4a RH, 2.88; CI, 1.09 to 7.60; P=0.03) in terms of magnitude of RH was higher than that of CBP (4b RH, 2.94; CI, 1.32 to 6.55; P=0.009; 4a RH, 2.06; CI, 1.02 to 4.15; P=0.04). On the other hand, the risk in groups 2a and 3a was not significantly different from that in group 1 by the CBP-based classification (group 2a RH, 0.94; CI, 0.50 to 1.77; P=0.8; group 3a RH, 0.75; CI, 0.35 to 1.62; P=0.5), and no stepwise increase in risk was observed (trend P=0.1).

However, when based on HBP classification, a significant increase in risk was clearly observed even in group 3a (RH, 2.40; CI, 1.09 to 5.29; P=0.03), and the stroke or TIA risk was increased linearly (trend P=0.01).

The same results were obtained when SAH was included in the stroke incidence (data not shown). The relationships between cerebral infarction and JNC-7 classification or cerebral hemorrhage and JNC-7 classification were analyzed separately. In cerebral infarction, the same results were observed, whereas in cerebral hemorrhage, such tendency was not observed (group 4a and 4b P>0.05). There was no interaction between use of antihypertensive medication and BP category (CBP P=0.4; HBP P=1.0).

Discussion
We found that JNC-7 classification by HBP had stronger predictive power than by CBP for stroke or TIA risk in this prospective cohort study. We also showed that risk for stroke was apparently predicted when HBP was used for classification irrespective of the presence of cardiovascular disease risks but not necessarily when CBP was used. These results were based on a comprehensive follow-up system in the
cerebral infarction, was not associated with JNC-7 classi-

fication; this may be attributable to the low incidence of cerebral hemorrhage (n=28).

In addition, the criteria categorized by CBP are not equivalent to those categorized by HBP. It should be emphasized that HBP was a better predictor of stroke and TIA than CBP. Thus, the usefulness of HBP should be higher in countries with high incidences of stroke and TIA, including Japan.

The JNC-VI and JNC-7 set the reference value of hypertension as HBP of 135/85 mm Hg.2,3 In the present study, HBP was classified on the basis of the percentage distribution of subjects according to the corresponding ratio of CBP. The HBP group 2 would be equivalent to prehypertension by JNC-7 on the basis of CBP because a stepwise increase of stroke risk occurred from group 1 to groups 3a and 3b. Such stepwise increase in stroke risk supports the concept of the JNC-7 recommendation that prehypertensive individuals have a relatively higher cardiovascular disease risk when compared with individuals with normal or "optimal"14 BP. These data also support the

<table>
<thead>
<tr>
<th>Variables Group 1</th>
<th>Group 2a</th>
<th>Group 2b</th>
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<th>Group 3b</th>
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<td>24.4±3.2</td>
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<td>Male (%)</td>
<td>28.9</td>
<td>25.8</td>
<td>58.8</td>
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<td>34.9</td>
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<td>Body mass index (kg/m²)</td>
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<td>23.7±3.2</td>
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<td>24.0±3.7</td>
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<td>PH of cardiovascular diseases (%)</td>
<td>1.1</td>
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<td>2.2</td>
<td>N/A</td>
<td>2.6</td>
<td>N/A</td>
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<td>Diabetes (%)</td>
<td>9.2</td>
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<td>32.9</td>
<td>N/A</td>
<td>31.6</td>
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<td>Smoking (%)</td>
<td>19.5</td>
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<td>55.1</td>
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<td>Hypercholesterolemia (%)</td>
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<td>31.4</td>
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<td>Home DBP (mm Hg)</td>
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<td>Casual SBP (mm Hg)</td>
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*See Table 1 for the definitions of groups.
Values are expressed as mean±SD.
PH indicates past history.

Ohasama cohort. First, our investigators repeatedly checked the medical records in Ohasama hospital with the radiologists’ interpretations of CT/MRI and were convinced that the diagnoses of stroke and subtypes were highly reliable. Second, the determination of stroke incidence by death certificates only was limited to 3% of the total cases, therefore, bias in the findings attributable to unidentified cases would be unlikely.

Japanese mortality resulting from stroke is 3× higher than that in the United States,13 and the mortality from coronary heart disease in Japan is one third of that in the United States.14 Such differences may be explained by differential environmental and genetic risk factors, and thus guidelines for treating hypertension would depend on the properties of each population. JNC-7 is essentially the guideline for the US population. However, our results demonstrate that JNC-7 criteria are valuable for prediction of stroke risk even in the general Japanese population. The incidence of first cerebral hemorrhage, contrary to that of cerebral infarction, was not associated with JNC-7 classifi-
intervention strategy for primary prevention of cardiovascular disease in prehypertensive individuals. This intervention might be based on HBP information because stroke risk in patients without cardiovascular disease risks is predictable only when based on HBP not on CBP.

In this and previous studies, we report repeatedly that HBP is superior to CBP at predicting prognosis of hypertension. Such beneficial characteristics of HBP may be derived from increased BP information obtained in relation to time of day. If HBP is measured once every morning and once every evening, this provides at least 60 measurements per month linked to specific times. Information on BP as a function of clock time, as well as an increased number of measurements, improves the quality of data. Furthermore, HBP is usually measured under more controlled conditions than CBP. The measurement conditions described here accord with the Japanese Society of Hypertension Guidelines for Self-Monitoring of Blood Pressure at Home, which may give high reproducibility and reliability of BP information without biases such as white-coat effect, regression dilution biases, and time effect. It is clinically difficult to exclude such biases using CBP. As a result, the CBP-based evaluation of individual risk was unstable (ie, in the present study, the number of subjects in each group using HBP was not matched to a comparable number of CBP subjects in relation to JNC-7). We postulate that such characteristics of HBP provide higher predictability of cardiovascular morbidity and mortality than those of CBP.

We validated the JNC-7 criteria for prediction of stroke risk in the general Japanese population and demonstrated that JNC-7 classification based on HBP measurements is a valuable tool for predicting morbidity and mortality of stroke and TIA. We conclude that HBP measurements should be used more extensively in clinical and epidemiological settings for the primary prevention of cerebrovascular diseases.

Figure 1. Risk of first stroke among 4 groups defined on the basis of HBP or CBP values. Right and left panels demonstrate RH and 95% CIs for first stroke adjusted for age, sex, and cardiovascular disease risks (diabetes mellitus, hypercholesterolemia, habitual smoking, or history of cardiovascular diseases) plotted on a log scale among groups classified by CBP and HBP values, respectively. Group 2, Prehypertension; group 3, stage 1 hypertension; group 4, stage 2 hypertension. Criteria are shown in Table 1. Group 1, normotension, is treated as the reference category. Solid squares are centered on the RH point and are sized in proportion to the number of events observed. Vertical lines extending from squares represent 95% CI. Trend probability values express the linearity among groups.

Figure 2. Risk of first stroke among groups defined on the basis of HBP or CBP values and cardiovascular risks. Right and left panels demonstrate RH and 95% CIs for first stroke adjusted for age and sex plotted on a log scale among groups classified by CBP and HBP values, respectively. Group 2, Prehypertension; group 3, stage 1 hypertension; group 4, stage 2 hypertension. Groups 2 through 4 were divided into 2 subgroups (a and b): those without and with high cardiovascular disease risks, respectively. Criteria are shown in Table 1. Group 1, normotension, is treated as the reference category. Solid squares are centered on the RH point and are sized in proportion to the number of events observed. Vertical lines extending from squares represent 95% CI. Trend probability values express the linearity among each subgroup (both with group 1).

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Stroke. 2004;35:2356-2361; originally published online August 26, 2004;
doi: 10.1161/01.STR.0000141679.42349.9f
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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