Predictive Value of Home Blood Pressure Measurement in Relation to Stroke Morbidity: A Population-Based Pilot Study in Ohasama, Japan


We investigated the utility of home blood pressure measurements for determining the risk of stroke. We also analyzed the relationship between home blood pressure and the incidence of stroke. Home blood pressure and screening blood pressure measurements were obtained from 1,789 residents (aged 40 yr or older) of a rural Japanese community. Blood pressure was measured at home with a semiautomatic device. A mean (±SD) of 23.0 ± 7.5 measurements were made for each subject. Subjects without a history of stroke and who were not receiving medication for hypertension (n = 1,256) were prospectively followed up for 4.4 ± 2.1 yr. Subjects were subdivided into quintiles according to their baseline blood pressure. The association between the baseline blood pressure and the incidence of the first-ever stroke was examined with the Cox proportional hazards regression model, adjusted for age and sex. The lowest risk of stroke morbidity occurred in the subjects in the third quintile for home systolic blood pressure (117-123 mmHg) and in those in the second quintile for home diastolic blood pressure (66-70 mmHg). The subjects in the fifth quintiles for home systolic (≥133 mmHg) and diastolic blood pressure (≥81 mmHg) had a significantly increased risk of stroke morbidity. The subjects in the first and the second quintiles for home systolic blood pressure and those in the first quintile for home diastolic blood pressure tended to have an increased risk as compared with subjects in the lowest risk groups, although this increase was not statistically significant, indicating two possibilities: a trend toward a J-shaped relationship or no decrease in risk of the first-ever stroke in subjects with home blood pressure level less than 123/70 mmHg. This relationship was not observed for screening blood pressure. We conclude that home blood pressure measurements can provide additional prognostic information to that obtained from blood pressure measurement in a medical environment. (Hypertens Res 1997; 20: 167-174)

Key Words: blood pressure, home measurements, screening measurements, stroke, prospective study

Longitudinal studies showing a relationship between blood pressure (BP) and cardiovascular diseases have been based on casual (office, clinic, or screening) BP measurements. However, the casual BP may not accurately reflect an individual’s usual BP outside a medical setting, because of the white-coat phenomenon, circadian variations, random variations, and the few measurements taken. Thus, casual BP measurements may not accurately predict an individual's risk of cardiovascular disease. Home BP measurements and ambulatory BP monitoring provide multiple measurements outside a medical environment; thus, these measurements are more likely to reflect an individual's “true” BP and to provide a more accurate basis for predicting the risk of cardiovascular disease than casual BP (1, 2).

Several studies have found that BP measurements obtained outside a medical setting show a better correlation with target-organ damage (3-7), and that ambulatory BP monitoring is a better predictor of the risk of cardiovascular disease than casual BP (8-12). However, the usefulness of home BP measurements for the prediction of cardiovascular morbidity and mortality has not been investigated.

We initiated home BP measurements in the general population of Ohasama, a rural Japanese...
community (13), and we have been monitoring the incidence of stroke in this cohort since 1987. Stroke remains a major cause of death as well as of dementia and disability in Japan. It is generally accepted that hypertension is associated with an increased risk of first-ever stroke and that the control of hypertension reduces this risk (14). These conclusions are derived from the results of observational and interventional studies based on casual BP measurements. Therefore, in the present study we examined the relationship between home BP measurements and the incidence of first-ever stroke in this general Japanese population, which included both normotensive and hypertensive subjects.

Subjects and Methods

Study Population

The present study is based on longitudinal observations of subjects who have been participating in the home BP measurement project in Ohasama, Iwate Prefecture, Japan since 1987. Ohasama is a rural community that had a total population of 8,040 in 1991. The socioeconomic and demographic characteristics of this region and the details of this project were previously reported (13). The most frequent cause of death among the residents of this town was cerebrovascular disease, followed by cancer and heart disease. As compared with the mortality in Japan, the standardized mortality ratio (SMR) of the residents of Ohasama Town between 1988 and 1992 was 0.98 for all-cause, 1.31 for cerebrovascular disease, 0.99 for cancer, and 0.59 for heart disease.

Home BP measurements were initiated in residents 8 yr of age or older in three out of four districts of Ohasama in 1987. In the present study, subjects younger than 40 yr of age were excluded because of a low incidence of hypertension-related disease and death. The total population of these three regions was 4,774. Of these residents, 2,716 were aged 40 yr or older at baseline (1,242 men aged 58.1 ± 13.1 yr and 1,474 women aged 60.1 ± 13.3 yr). We excluded 575 subjects because they were working outside the town (394 men aged 52.4 ± 11.0 yr and 181 women aged 49.8 ± 7.5 yr). This exclusion was necessary because our project also included ambulatory BP measurements (15), which required that the subjects stayed in the town during daytime working days to allow us to equip them with a device for ambulatory BP monitoring.

Among the remaining 2,141 subjects, those who were hospitalized (n = 121) or who had dementia or were bedridden (n = 31) were also excluded from the study. A total of 1,989 subjects (781 men aged 62.1 ± 11.2 yr and 1,208 women aged 61.4 ± 10.9 yr) were eligible for the study. The eligible subjects comprised mainly farmers, housewives, and retired individuals. Informed consent to participate in the study was obtained from 1,957 (96%) of these 1,989 subjects; 32 individuals declined to participate. At least three home BP measurements (on 3 separate days) and screening BP measurements were obtained from 1,789 individuals (720 men and 1,069 women) during the study period. Subjects who were taking antihypertensive medication, who had a history of stroke, or who had atrial fibrillation were excluded (n = 533), but those who had other major chronic diseases, such as diabetes mellitus or coronary heart disease, were included unless they met other exclusion criteria. Therefore, we analyzed data from 1,256 subjects (507 men aged 59.1 ± 11.0 yr and 749 women aged 58.3 ± 9.9 yr). Information on antihypertensive medication was obtained both from questionnaires sent to residents at the time of home BP measurements and from medical records at Ohasama Prefectural Hospital. Subjects were followed up for 4.4 ± 2.1 yr (range, 1 to 83 months).

Those who participated in the study (n = 1,256) and those who did not (because of the reasons described above; n = 1,460) had similar levels of school education. The SMR of the study participants between 1988 and 1992 as compared with the non-participants was 0.83 for overall mortality, which was not statistically significant. Thus, selection bias with respect to the study subjects was unlikely, and the study subjects well represented the residents of this community.

This study was approved by the Institutional Review Board of Tohoku University School of Medicine and by the Department of Health of the Ohasama Town government.

Home Blood Pressure Measurements

Physicians, public health nurses, or both instructed subjects on the proper way to measure BP at home. Subjects were asked to measure and record their BP every morning within 1 h of waking for 4 wk (13). They were instructed to measure BP in the sitting position using the non-dominant arm after at least 2 min of rest. The average of these recordings was used as the baseline home BP measurement. Data from subjects who measured BP at home more than three times (on 3 separate days) during the 4-wk study period were included in the analysis. We had previously found that the mean BP obtained at home on the first three days was not significantly different from the mean BP obtained at home over the entire study period (13). The mean number of home BP measurements per subject was 23.0 ± 7.5.

The semi-automatic device used for home BP measurements (HEM 401C; Omron Life Science Co. Ltd., Kyoto, Japan) is based on the cuff-oscillographic principle (16) and generates a digital display giving the systolic BP, diastolic BP, and pulse rate. A standard arm cuff was used.

Screening Blood Pressure Measurements

Subjects received health examinations after home BP measurements were done. Physicians or nurses measured BP with the use of a fully automatic device. Blood pressure was measured twice consecutively while each subject was in the sitting position after at least 2 min of rest, and the average of these two values was considered the baseline screening BP and was used for analysis. Screening BP measurements were made using a USM 700 F (Ueda Electronic Works Co. Ltd., Tokyo, Japan),

168  Hypertens Res Vol. 20, No. 3 (1997)
an automatic BP measuring device based on the Korotkoff sound technique (the microphone method).

The BP measuring devices used in the present study have been validated (16). All devices used met the criteria of the Association for the Advancement of Medical Instrumentation (17).

**Definition of Stroke**
Information on cerebrovascular events was obtained from death certificates, the stroke registry, and a questionnaire distributed to each household every year. If a subject was suspected of having had a stroke, we visited the hospital to which he or she had been referred and inspected the medical records and brain computed tomographic (CT) scans or magnetic resonance images (MRI) when available.

The diagnosis of stroke was based on the occurrence of clinical signs of focal or global disturbances in cerebral function that lasted more than 24 h or that resulted in death. Patients were classified into the following stroke subtypes on the basis of clinical signs, brain imaging examinations, or both: cerebral hemorrhage, cerebral infarction, subarachnoid hemorrhage, or undetermined type. Cerebral hemorrhage was defined as the rapid evolution of focal neurological signs, a rapid progression to coma, signs of meningeal irritation, an elevated blood pressure, headache, and the presence of blood in cerebrospinal fluid. Cerebral infarction was diagnosed if there was a slow development of focal neurologic signs lasting more than 24 h, a relative preservation of consciousness, and the absence of blood in cerebrospinal fluid. A diagnosis of subarachnoid hemorrhage was based on the sudden onset of severe headache with only a relatively momentary disturbance of consciousness, signs of meningeal irritation, subhyaloid hemorrhage, the absence of focal neurological signs, and the presence of blood in the cerebrospinal fluid. Strokes were assigned to the "undetermined" category if the onset and the residual deficit were sufficiently well documented to suggest a high probability of stroke but clinical data were insufficient to allow further categorization of the type of stroke. The diagnosis was confirmed by CT or MRI findings, or both when available.

**Analysis of Data**
The relationships between baseline home and screening BP and the incidence of stroke were investigated. Residence in Ohasama as of December 31, 1994 was confirmed by the residents' registration cards. These cards are accurate and reliable in Japan because they are the basis for obtaining pension and social security benefits. Only two subjects (0.2% of the study subjects) moved away and were lost to follow-up. There were 57 deaths (4.5% of the study subjects), which were identified from the registration cards. Death certificates were obtained from the Ohasama Health Department. Deaths resulted from strokes in 13 subjects and from non-stroke-related causes in 44 subjects, including 6 cardiovascular deaths (death from myocardial infarction or heart failure) and 38 non-cardiovascular deaths.

The association between baseline BP and stroke morbidity was analyzed by Kaplan-Meier life-table analysis (18) using the SAS LIFETEST procedure (19) and the Cox proportional hazards regression model (20) performed with the SAS PHREG procedure (19). The dependent variable in these analyses was the number of days from the first BP measurement to the occurrence of a stroke or censoring. Stroke-free subjects were censored as of December 31, 1994 or censored on the day of their deaths. The independent variables were age, sex, and BP. All information on the subjects was collected during the 4-wk baseline period, during which the home BP measurements were being taken.

Subjects were classified into four age groups at the time of the baseline BP measurements: 40 to 49, 50 to 59, 60 to 69, and 70 or more yr. The average of all home BP measurements and the average of two screening BP measurements were defined as the baseline BPs. For the baseline BP, we applied a quintile analysis, in which subjects were subdivided almost equally into five quintiles according to the distribution of baseline BPs. Estimates of the relative hazard (RH) for each variable and the 95% confidence interval (95% CI) were derived from the coefficient and its standard error of the Cox proportional hazards model. In all analyses, we treated the baseline BP level with the lowest morbidity risk as the reference category. Data are expressed as the mean ± SD. A level of p < 0.05 was considered as statistically significant.

**Results**
The mean home systolic BP level in 1,256 subjects was 121.9 ± 14.0 mmHg (range, 86 to 177 mmHg); the mean home diastolic BP level was 73.5 ± 10.0 mmHg (range, 43 to 110 mmHg). The mean screening systolic BP level was 130.7 ± 18.6 mmHg (range, 83 to 215 mmHg); the mean screening diastolic BP level was 74.8 ± 11.3 mmHg (range, 42–113 mmHg). The mean systolic and diastolic screening BPs were significantly higher than home BP levels (p < 0.001).

First-ever strokes were identified in 39 (26 men and 13 women) of 1,256 subjects (23 cases of cerebral infarction, 9 cases of cerebral hemorrhage, 6 cases of subarachnoid hemorrhage, and 1 case of undetermined type). CT or MRI findings were available for 30 of the 39 subjects (76.9%). Table 1 shows the number of cases for the first-ever stroke stratified by age. The total incidence of stroke increased with advancing age.

Kaplan-Meier survival curves showed a significant difference in the stroke-free survival rate according to the home diastolic BP (Fig. 1A, log-rank χ² = 18.8, p < 0.001). Subjects in the fifth quintile for home diastolic BP level (BP ≥ 81 mmHg) had the lowest stroke-free survival rate. Similarly, there was a significant difference in stroke-free survival according to the screening diastolic BP (Fig. 1B,
log-rank $\chi^2 = 10.2$, $p < 0.05$).

The Cox proportional hazards model demonstrated that the fifth quintiles for home systolic and diastolic BP were associated with the highest risk of stroke morbidity (Table 2). Subjects in the fourth quintile of home systolic BP also had a statistically significant increase in risk. The lowest risk of stroke morbidity was observed in subjects in the third...
quintile for home systolic BP and in those in the second quintile for home diastolic BP. Subjects with home systolic BP $\geq 116$ mmHg and home diastolic BP $\geq 65$ mmHg tended to have an increased risk as compared with subjects in the third quintile for home systolic BP and those in the second quintile for home diastolic BP, respectively. However, these results were not statistically significant.

The RHs of BPs were highest for subjects in the fifth quintile of the screening systolic and diastolic BP. The RHs of the screening diastolic BP were lowest for the first quintile. There was a positive linear relationship between screening diastolic BP and stroke morbidity. However, no consistent association was observed between screening systolic BP and stroke morbidity (Table 3).

The actual number of strokes in each quintile of home BP is illustrated in Fig. 2. The incidence of cerebral infarction was more frequent in the fifth quintile of home diastolic BP, being followed by the first and the forth quintiles, and there was no case of cerebral infarction in the third quintile of home systolic BP. We, therefore, re-assessed the relationship between the home diastolic BP and cerebral infarction using the Cox proportional hazards model (Fig. 3). The RHs and 95% CIs indicated that subjects with home diastolic BP between 71 and 74 mmHg (the third quintile) had the lowest risk of cerebral infarction. Subjects in the fifth quintile ($\geq 81$ mmHg) had a significantly higher risk of cerebral infarction as compared with subjects in the third quintile. The risk of cerebral infarction tended to be higher in subjects with home diastolic BPs $\leq 70$ mmHg.

### Table 3. Relationship between Screening Blood Pressure and First-Ever Stroke Incidence, Analyzed by the Cox Proportional Hazards Model, Adjusted for Age and Sex

<table>
<thead>
<tr>
<th>Home blood pressure (mmHg)</th>
<th>Subjects (N)</th>
<th>Events (N)</th>
<th>Relative Hazard</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systolic blood pressure quintile</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st $\leq 114$</td>
<td>235</td>
<td>3</td>
<td>1.68</td>
<td>0.34 - 8.40</td>
</tr>
<tr>
<td>2nd 115-125</td>
<td>267</td>
<td>9</td>
<td>3.56</td>
<td>0.96 - 13.17</td>
</tr>
<tr>
<td>3rd 126-132</td>
<td>232</td>
<td>5</td>
<td>2.24</td>
<td>0.53 - 9.39</td>
</tr>
<tr>
<td>4th 133-143</td>
<td>268</td>
<td>3</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>5th $\geq 144$</td>
<td>254</td>
<td>19</td>
<td>6.04</td>
<td>1.77 - 20.60</td>
</tr>
<tr>
<td><strong>Diastolic blood pressure quintile</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st $\leq 64$</td>
<td>231</td>
<td>2</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>2nd 65-70</td>
<td>249</td>
<td>7</td>
<td>2.89</td>
<td>0.60 - 13.94</td>
</tr>
<tr>
<td>3rd 71-76</td>
<td>264</td>
<td>7</td>
<td>2.79</td>
<td>0.58 - 13.44</td>
</tr>
<tr>
<td>4th 77-83</td>
<td>241</td>
<td>7</td>
<td>2.70</td>
<td>0.56 - 13.03</td>
</tr>
<tr>
<td>5th $\geq 84$</td>
<td>271</td>
<td>16</td>
<td>6.12</td>
<td>1.40 - 26.70</td>
</tr>
</tbody>
</table>

**Fig. 2.** Distribution of subtypes of stroke for each quintile of baseline home systolic (A) and diastolic (B) blood pressure levels.
Discussion

Despite several decades of studies, the clinical utility of home BP measurements has not been established, because the predictive value of home BP measurements has not been fully evaluated and because there are no established reference values for home BP measurements to define normotension and hypertension. The prognostic usefulness and reference values of home BP measurements should be determined by studies investigating the risk of morbidity and mortality from hypertension-related complications. Thus, longitudinal observation of a population is required to determine the predictive value of home BP measurements. We have reported that the predictive power of the home BP level for subsequent all-cause mortality was stronger than that of casual-screening BP (21). The present study is the first to investigate the predictive value of home BP measurements for stroke morbidity.

The present study demonstrated that both home and screening BP measurements predicted the incidence of the first-ever stroke. For systolic BP, the risk of stroke was the highest in the subjects with home systolic BP $\geq 124$ mmHg and screening systolic BP $\geq 144$ mmHg. This result is consistent with most results of the previous studies in which home BP was much lower than screening BP (2, 13, 22, 23). For diastolic BP, the risk was the highest in the subjects with home diastolic BP $\geq 84$ mmHg and screening diastolic BP $\geq 81$ mmHg. The difference between home and screening diastolic BPs was smaller than that between systolic BPs. This is mainly due to the similar distributions of diastolic BP for home and screening measurements (13).

Screening BP measurements, which are affected by a number of factors including the white-coat phenomenon, the orientation response, and observer bias, tend to be higher than home BP measurements. However, casual or screening BP measurements have been found to predict the outcome of hypertension in the population at large (24-27), suggesting that a reactive pressor response or BP variability per se contributes to cardiovascular morbidity and mortality (11, 28). Screening (casual) BP measurements, however, do not necessarily estimate an individual’s usual BP levels and, thus, do not necessarily reflect the prognosis of hypertension in an individual. Home BP measurements can be done repeatedly under constant and controlled conditions and are unaffected by observer bias or the “white-coat” phenomenon. Therefore, the long-term reproducibility of home BP measurements may be superior to that of screening BP measurements (29).

Most previous observational and interventional studies showed a linear relationship between the BP level and cardiovascular morbidity and mortality (14, 30, 31). However, several interventional trials demonstrated a J-shaped relationship between the BP during antihypertensive treatment and the risk of cardiovascular events (32-35). Although these studies consistently showed a J-shaped relationship between cardiac events and diastolic BP, a J-shaped relationship between BP and stroke remains controversial (36, 37).

The frequency of stroke has been shown to increase linearly with increasing BP, suggesting that the lower the BP, the lower the rate of stroke morbidity and mortality (30, 38-41). However, Kario et al. (42) and Watanabe et al. (43) suggested that a marked nocturnal fall in BP in elderly hypertensive patients not receiving antihypertensive medication was accompanied by silent cerebrovascular damage. Similarly, Nakamura et al. (44) suggested that a nocturnal dip in BP in patients treated with anti-hypertensive drugs may accelerate the progression of ischemic brain lesions. Irie et al. (45) recently observed a J-shaped phenomenon between diastolic BP and stroke recurrence rate in patients receiving antihypertensive treatment. These findings suggest that an inappropriately low BP, regardless of whether or not the patients are treated with anti-hypertensive medication, increases the risk of ischemic cerebrovascular disease. In the present study, the subjects in the first and the second quintiles for home SBP and those in the first quintile for home DBP tended to have an increased risk of stroke as compared with subjects in the lowest risk group, although this increase was not statistically significant, indicating two possibilities: a trend toward a J-shaped relationship or no decrease in risk of the first-ever stroke in subjects with home BP levels less than 123/70 mmHg. Recently Glynn et al. reported that the J-shaped relationship between BP and cardiovascular mortality disappeared after excluding patients who died within the first few years of follow-up (31). Therefore, further observations are needed to establish a J-shaped relationship between home BP and cardiovascular morbidity.
The results of this study should be interpreted cautiously because of two study limitations.

First, since this was a preliminary analysis, known risk factors for stroke, such as smoking, past medical history, and serum cholesterol concentration, were not controlled.

Second, we used the baseline BP for the analysis and, therefore, changes in BP during the follow-up period were not taken into account. We are presently evaluating the effect and distribution of known risk factors for cardiovascular and cerebrovascular disease on the predictive value of home BP measurements.

Finally, we conclude that home BP measurements can provide additional prognostic information to that obtained from blood pressure measurement in a medical environment.

References