Prognosis of Isolated Systolic and Isolated Diastolic Hypertension as Assessed by Self-Measurement of Blood Pressure at Home

The Ohasama Study

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Background: Although the clinical significance of systolic-diastolic hypertension and isolated systolic hypertension has been established, the significance of isolated diastolic hypertension has not been fully investigated.

Objective: To clarify the prognostic significance of isolated systolic and isolated diastolic hypertension as assessed by self-measurement of blood pressure (BP) at home (home BP measurements), which has a better reproducibility and prognostic value than casual BP measurements in the general population.

Subjects and Methods: We obtained home BP measurements for 1913 subjects aged 40 years or older, then followed up their survival status (mean, 8.6 years). We classified the subjects into the following 4 groups according to their home BP levels: systolic-diastolic hypertension, isolated systolic hypertension, isolated diastolic hypertension, and normotension. The prognostic significance of each type of hypertension for the risk of cardiovascular mortality risk was investigated using a Cox proportional hazards regression model adjusted for possible confounding factors.

Results: The risk for isolated systolic hypertension and systolic-diastolic hypertension were significantly higher than the relative hazard for normotension, while isolated diastolic hypertension was associated with no significant increase in risk. Home pulse pressure measurement was also independently associated with an increase in the risk of cardiovascular mortality.

Conclusions: Isolated diastolic hypertension, as assessed by home BP measurements, carried a low risk of cardiovascular mortality, similar to that found in subjects with normotension, suggesting that the prognosis of hypertension would be improved by treatment focused on systolic rather than on diastolic home BP measurements. To our knowledge, this study is the first to demonstrate the clinical significance of pulse pressure as assessed by home BP measurement.

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The diagnosis of hypertension is usually based on blood pressure (BP) criteria for both systolic and diastolic BP (SBP and DBP, respectively). However, some subjects fulfill only the SBP or only the DBP criteria. These subjects are categorized as having isolated systolic hypertension (ISH) or isolated diastolic hypertension (IDH). While the prognostic significance of ISH has been established by longitudinal intervention trials and meta-analysis, only 2 longitudinal studies investigated the prognostic significance of IDH. In these studies, the diagnosis of hypertension was based on casual or clinic measurements of BP. Casual BP measurement is known to have several limitations, such as poor reproducibility, the presence of a “white coat effect,” observer bias. Recently, the use of self-measurement of BP at home (hereafter referred to as “home BP measurement”), which has been reported to have a better reproducibility and prognostic value than casual BP measurement, has been acknowledged. The Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure and the 1999 World Health Organization-International Society of Hypertension Guidelines for the Management of Hypertension have also emphasized its usefulness. Since 1987, we have been conducting a prospective cohort study to investigate the relationship between home BP measurements and survival in the general population of Ohasama, Japan. The objective of this substudy was to clarify the prognostic significance of ISH and IDH, assessed using home BP measurements, in...
SUBJECTS AND METHODS

DESIGN

This study is part of a longitudinal observational study of subjects who have been participating in a BP measurement project in Ohasama, Japan, since 1987. The socioeconomic and demographic characteristics of this region and full details of the project have been described elsewhere.12,13 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

The selection of study subjects has been described previously.13 Briefly, the subjects were aged 40 years or older and residents of 3 of the 4 regions of Ohasama (N=2716). Hospitalized persons (n=121) and persons with dementia or who were bedridden (n=31) were excluded from the study. Individuals who worked out of town (n=575) were also excluded because the project involved ambulatory BP monitoring. Informed consent to participate in the study was given by 1957 of 1989 eligible subjects. Home BP measurements were obtained from 1913 subjects who collected their own data on more than 3 occasions (3 days) during the 4-week study period. This criterion was based on our previous observation that the average BP value for the first 3 days did not differ significantly from values obtained during the entire study period.13 Therefore, the study population consisted of 1913 individuals (mean age, 61.0 years; men–women ratio, 40:60) representing 90% of the total eligible population. We have previously confirmed that these subjects were representative of the total population.13

HOME BP MEASUREMENTS

In our study, we used the following procedure to ascertain the accuracy of home BP measurements. First, physicians and public health nurses conducted a health education class to inform the population about home BP recording and to teach them how to measure their BP. Then, we checked whether they were able to measure their BP correctly. Eighty percent of households in this town attended the class, and public health nurses visited all of the remaining households to provide instruction on home BP measurement and to check whether they were able to measure their BP correctly. These procedures were also described in detail in our previous articles.13,14 The subjects were then asked to measure their BP every morning and to record the results for 4 weeks. Measurements were obtained within 1 hour of awaking and before breakfast, with the subject seated and having rested for at least 2 minutes. In subjects receiving antihypertensive drugs, home BP was measured before taking the drugs. The home BP of an individual was defined as the mean of all measurements obtained for that person. The mean (±SD) number of home BP measurements was 20.8 ± 8.3 (range, 3–38).

SCREENING (CASUAL) BP MEASUREMENTS

Free annual health checkups, including BP measurements, are available for all persons aged 40 years or older. Using a semiautomatic device, a nurse or technician took 2 consecutive BP measurements with the subjects seated, after at least 2 minutes of rest. The screening BP was defined as the average of these 2 readings. Of the 1913 study subjects, 1789 (90%) had a health checkup during the year in which they were taking home BP measurements. There was no statistically significant difference in mean age, sex distribution, or mean home measurements of SBP and DBP between those who participated in screening and those who did not.

RESULTS

The mean duration of follow-up was 8.6 years (maximum follow-up, 11.7 years). There were 93 deaths (4.8%) owing to CVD and 172 deaths (9.0%) of a non-CVD cause. Of the 93 deaths owing to CVD, 55 (59%) were due to stroke and 38 (41%) were due to heart disease. Twenty-two subjects (1.2%) moved away from the region and were lost to follow-up.

Of the 1913 study subjects, 402 (23%) were classified as current or ex-smokers, 301 (22%) were classified as obese, and 598 (31%) were taking antihypertensive medication. A history of CVD, hypercholesterolemia, or diabetes mellitus was identified in 74 subjects (4%), 224 subjects (13%), and 229 subjects (13%), respectively. Mean home BP measurements were 125.5 ± 11.3 mm Hg for SBP and 75.1 ± 10.0 mm Hg for DBP. The mean home pulse pressure (PP) was 50.3 ± 10.3 mm Hg.

The Table lists the characteristics of the subjects in each group, classified on the basis of home BP measurements. Subjects with IDH were significantly younger, while subjects with ISH were significantly older than all of the study subjects. Men and smokers were more preponderant in the IDH group, while women and non-smokers were more preponderant in the ISH group. Mean SBPs were higher in subjects with SDH (148.7 ± 9.6 mm Hg) or ISH (144.9 ± 7.9 mm Hg) than in those with IDH (130.1 ± 4.5 mm Hg) or NT (118.3 ± 9.7 mm Hg), while mean DBPs were higher in subjects with SDH (91.4 ± 6.1 mm Hg) and subjects with IDH (87.4 ± 4.0 mm Hg) than in subjects with ISH (76.5 ± 5.1 mm Hg) and subjects with NT (70.9 ± 7.1 mm Hg). Mean home PPs were higher in subjects with ISH (68.4 ± 8.9 mm Hg) or SDH (57.3 ± 9.4 mm Hg) than those with IDH (42.7 ± 5.2 mm Hg) or NT (47.5 ± 7.4 mm Hg).

PROGNOSTIC VALUE OF THE TYPE OF HYPERTENSION AS ASSESSED BY HOME BP MEASUREMENTS

We investigated the relationship between the type of hypertension and CVD mortality among the entire study population. Cardiovascular disease death rates per 100 person-years were higher in subjects with SDH (1.11) or ISH (2.04) than in subjects with NT (0.33) or IDH (0.26).
The RHs for CVD mortality were also significantly higher in subjects with SDH (RH = 1.85; 95% CI, 1.07-3.21; P = .03) or ISH (RH = 2.35; 95% CI, 1.41-3.90; P = .001) than in subjects with IDH (RH = 1.09; 95% CI, 0.33-3.59; P = .89) or NT.

Since antihypertensive treatment would have affected the prognosis, we analyzed the relationship between the type of hypertension and CVD mortality in subjects who were taking antihypertensive medication (treated subjects) and those who were not (untreated subjects), separately. The results demonstrated a similar tendency to those observed in the analysis of the entire study population.

Among untreated subjects, CVD death rates per 100 person-years were higher in subjects with SDH (1.01) or ISH (1.64) than in subjects with NT (0.24) or IDH (0.14). The RHs for CVD mortality were also higher in subjects with SDH (RH = 1.94; 95% CI, 0.85-4.44; P = .12) or ISH (RH = 2.42; 95% CI, 1.09-5.37; P = .03) than in subjects with IDH (RH = 1.57; 95% CI, 0.20-12.27; P = .67) or NT.

Treated subjects showed almost the same tendency for the relationship between the type of hypertension and CVD risk, ie, CVD death rates per 100 person-years were higher in subjects with SDH (1.18) or ISH (2.32) than in subjects with NT (0.65) or IDH (0.41). The RHs for CVD mortality were also higher in subjects with SDH (RH = 1.86; 95% CI, 0.87-3.97; P = .11) or ISH (RH = 2.42; 95% CI, 1.22-4.79; P = .001) than in subjects with IDH (RH = 0.98; 95% CI, 0.22-4.37; P = .75) or NT.

Since the subjects with NT and IDH were younger than those with SDH and ISH, we also analyzed the 2 age groups separately, ie, middle-aged (40-64 years) and elderly (≥65 years) subjects. A similar tendency was also observed when we analyzed the relationship between CVD mortality and the type of hypertension in middle-aged subjects and elderly subjects. For the middle-aged group, the CVD mortality rates per 100 person-years were higher in subjects with SDH (0.49) or ISH (0.67) than in those with NT (0.10) or IDH (0.10). Similarly, among the elderly subjects, CVD mortality rates per 100 person-years were higher in subjects with ISH (2.67) or SDH (1.86) than in subjects with IDH (1.19) and NT (1.00).

Systolic-diastolic hypertension and ISH were associated with a higher CVD mortality rate per 100 person-years than IDH and NT in both men and women (men/women with SDH, 0.85/1.55; men/women with ISH, 3.93/0.98; men/women with IDH, 0.00/0.81; and men/women with NT, 0.46/0.27).
Descriptive Data Among All Subjects in Each Hypertension Type Assessed by Home Blood Pressure Measurements*

<table>
<thead>
<tr>
<th>Factor</th>
<th>NT</th>
<th>IDH</th>
<th>ISH</th>
<th>SDH</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>1360</td>
<td>132</td>
<td>179</td>
<td>242</td>
<td></td>
</tr>
<tr>
<td>Age, mean ± SD, y</td>
<td>59.1 ± 10.8</td>
<td>55.4 ± 9.3</td>
<td>71.6 ± 9.5</td>
<td>65.4 ± 10.0</td>
<td>.001†</td>
</tr>
<tr>
<td>Sex, % female</td>
<td>64.6</td>
<td>32.6</td>
<td>59.8</td>
<td>33.1</td>
<td>.001†</td>
</tr>
<tr>
<td>Smoking</td>
<td>20.4</td>
<td>40.9</td>
<td>17.9</td>
<td>33.1</td>
<td>.001†</td>
</tr>
<tr>
<td>Obesity</td>
<td>19.0</td>
<td>24.2</td>
<td>22.4</td>
<td>25.6</td>
<td>.07‡</td>
</tr>
<tr>
<td>Antihypertensive treatment</td>
<td>21.9</td>
<td>40.2</td>
<td>56.4</td>
<td>60.3</td>
<td>.001†</td>
</tr>
<tr>
<td>History of CVD</td>
<td>2.9</td>
<td>4.6</td>
<td>7.3</td>
<td>6.2</td>
<td>.06‡</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>10.6</td>
<td>14.0</td>
<td>11.4</td>
<td>16.5</td>
<td>.046‡</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>11.0</td>
<td>14.4</td>
<td>10.6</td>
<td>17.4</td>
<td>.03‡</td>
</tr>
<tr>
<td>Home SBP, mean ± SD, mm Hg</td>
<td>118.3 ± 9.7</td>
<td>130.1 ± 4.5</td>
<td>144.9 ± 7.9</td>
<td>148.7 ± 9.6</td>
<td>.001†</td>
</tr>
<tr>
<td>Home DBP, mean ± SD, mm Hg</td>
<td>70.9 ± 7.1</td>
<td>87.4 ± 4.0</td>
<td>76.5 ± 5.1</td>
<td>91.4 ± 6.1</td>
<td>.001†</td>
</tr>
<tr>
<td>Home pulse pressure, mean ± SD, mm Hg</td>
<td>59.1 ± 10.8</td>
<td>42.7 ± 5.2</td>
<td>68.4 ± 8.9</td>
<td>57.3 ± 9.4</td>
<td>.001†</td>
</tr>
</tbody>
</table>

* NT indicates subjects with normotension, ie, a systolic blood pressure (SBP) lower than 137 mm Hg and a diastolic blood pressure (DBP) lower than 84 mm Hg. IDH, subjects with isolated diastolic hypertension, ie, an SBP lower than 137 mm Hg and a DBP of 84 mm Hg or higher; ISH, subjects with isolated systolic hypertension, ie, an SBP of 137 mm Hg or higher and a DBP lower than 84 mm Hg; SDH, subjects with systolic-diastolic hypertension, ie, an SBP of 137 mm Hg or higher and a DBP of 84 mm Hg or higher; and CVD, cardiovascular disease. Values are given as percentage of subjects unless otherwise indicated.
† Analysis of variance.
‡χ² Test.

PROGNOSTIC VALUE OF HOME PP MEASUREMENTS

Although there was little difference in SBP between subjects with SDH and subjects with ISH, the RH in subjects with ISH was higher than that in subjects with SDH. Furthermore, the risk of subjects with IDH who had the minimal PP was similar to that in subjects with NT despite the higher SBP in subjects with IDH. This finding suggests that home PP measurement is also an important prognostic factor for CVD. Therefore, we analyzed the relationship between CVD mortality and home PP as a continuous variable, instead of stratifying PP by the presence or absence of antihypertensive treatment.

We also analyzed the relationship between CVD mortality and the type of hypertension assessed by screening BP measurements. For this analysis, we classified the subjects into 4 groups according to their screening BP levels, using 140/90 mm Hg as criteria to define hypertension.

Isolated systolic hypertension tended to be associated with a higher RH (RH=1.49; 95% CI, 0.89-2.47; P=.13) and CVD mortality rate (0.94 per 100 person-years) than NT (mortality rate=0.35 per 100 person-years). This relationship was also observed when the subjects with IDH (RH=1.20; 95% CI, 0.16-8.96; P=.86, mortality rate=0.39 per 100 person-years) was compared with subjects with NT. Furthermore, screening PP values were not significantly related to the risk of CVD mortality (RH=1.09; 95% CI, 0.94-1.27, P=.24, per 10-mm Hg increase).

COMMENT

This study was part of a longitudinal observation of a representative sample of the general population of a rural Japanese community. When assessed by home BP measurements, the result demonstrated that, compared with subjects with NT, subjects with ISH or SDH have a significantly higher risk of CVD mortality, while those with IDH do not. These findings were observed both in treated and untreated subjects, in young and elderly subjects, and in men and women.

Only 2 other studies have investigated IDH as a risk factor for CVD. Fang et al7 followed up 1560 middle-aged subjects with diastolic hypertension, and demonstrated that the risk of acute myocardial infarction was significantly higher in subjects with SDH than in those with IDH. Petrovitch et al8 followed up 7590 Japanese-American men among the general population of Hawaii and showed that, for middle-aged persons, the risk of a first symptomatic stroke was lower in subjects with IDH or NT than in subjects with ISH or SDH. Although these subjects were classified according to casual BP measurements, the same result, ie, a lower risk of CVD morbidity in subjects with IDH than in subjects with SDH, was observed as in this study, during which home BP measurements were used.

In the present analysis, we confirmed that the risk of CVD mortality was somewhat higher in subjects with ISH than in subjects with SDH, while IDH was associated with a lower risk than SDH or ISH. Thus, our results indicate that SBP, but not DBP, is a strong predictor of CVD mortality when assessed by home BP.
measurements. The prognostic value of SBP (as assessed by repeated casual BP measurements) has recently been confirmed by an investigation in an elderly Italian population.21

In our analysis based on home BP measurements, subjects with ISH or SDH, who also had an increased home PP than subjects with NT or IDH who had lower PP, were at higher risk of CVD mortality than the subjects with NT or IDH. In contrast, the risk in IDH did not differ significantly from that in NT. Systolic blood pressure was significantly higher in subjects with IDH than in subjects with NT; however, PP was somewhat lower in subjects with IDH, although the risks of CVD mortality were no different. Similarly, the CVD mortality risk was somewhat higher in subjects with ISH than in subjects with SDH, although SBP in ISH was similar to that in SDH. Furthermore, home PP were also significantly related to the mortality risk when analyzed as a continuous variable, independently of other risk factors for CVD mortality. These results are consistent with those of several previous studies investigating the relationship between PP and CVD mortality.7,22-27 and thus reconfirm the importance of PP in predicting the prognosis of hypertension. To our knowledge, this study is the first to demonstrate the clinical significance of PP as assessed by home BP measurement.

When we estimated the risk of CVD mortality in subjects with SDH, ISH, IDH, or NT, as classified by screening BP measurements, the risk tended to be higher in subjects with ISH than in those with NT, while subjects with SDH also had an increased home PP measurements. However, as the predictive power of multiple casual BP measurements is reported to be as high as that of ambulatory BP,28 it is difficult to obtain consecutive and multiple casual BP measurements within a certain period at screening or in daily clinical practice. We conclude that home BP measurement is beneficial because it facilitates multiple measurements over a certain period.

CONCLUSION

We demonstrated (1) that IDH is associated with a low risk of CVD mortality (similar to that observed in NT) while ISH carries a similarly high risk to SDH, and (2) that PP is a strong independent predictor of CVD mortality. These findings were made using home BP measurements, which have been confirmed to be a more reliable method of estimating the prognosis of hypertension in the general population than casual BP measurements. These results suggest that the prognosis of hypertension would be improved by treatment focused on SBP rather than on DBP. However, they do not mean that IDH is harmless, since it is possible that a younger adult with IDH may convert to ISH or develop SDH with increasing age. Further observational and interventional studies are, therefore, needed to clarify the clinical significance of IDH.

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