A STUDY OF LONG-TERM OBSERVATIONS
IN BORDERLINE HYPERTENSION

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To identify the risk factors of borderline hypertension in the development of established hypertension, the relationship between the changes in blood pressure over 10 years and the clinical features in the initial year was investigated in a Japanese urban population. The occurrence of cardiovascular complications in cases with borderline hypertension were also studied.

The prevalence of borderline hypertension in the initial year was 18.2%. On the basis of the blood pressure changes over 10 years, these subjects could be classified into the following 5 groups: (I) those with developing established hypertension, 19.0%; (II) those with fluctuating between hypertension and borderline hypertension, 27.4%; (III) those with remaining with borderline hypertension, 19.6%; (IV) those with fluctuating between borderline hypertension and normotension, 22.9%; (V) those with improving to normotension, 11.2%. The later development of established hypertension was found in only 2.4% of normotensives in the initial year.

Obesity and glucose intolerance were more frequently observed in group I (38.2% and 29.4%, respectively) than in the other groups. Diastolic blood pressures in the initial year were significantly higher in groups I and II than in III, IV and V.

As for the occurrence of cardiovascular complications during the observation period, electrocardiographic abnormalities and hypertensive and/or arteriosclerotic retinopathy were not infrequently observed even in borderline hypertensives.

Therefore, in subjects with borderline hypertension, continuous medical management, including correction of obesity as well as glucose intolerance, is necessary to prevent the development of established hypertension and subsequent cardiovascular complications.

Key Words: Borderline hypertension Glucose intolerance Obesity Cardiovascular complications

A group of experts of the National High Blood Pressure Education Program in the United States estimated that there are 16 million Americans with borderline hypertension. On the other hand, it has been pointed out that there are 15 million patients with borderline hypertension in Japan. Borderline hypertension has been well

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TABLE I  THE INCIDENCE OF NORMOTENSION, BORDERLINE HYPERTENSION AND HYPERTENSION IN THE INITIAL YEAR OF THIS STUDY

<table>
<thead>
<tr>
<th></th>
<th>No.</th>
<th>%</th>
<th>Age (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>106 (14)*</td>
<td>10.8</td>
<td>41.2 ± 7.0</td>
</tr>
<tr>
<td>Borderline hypertension</td>
<td>179 (12)*</td>
<td>18.2</td>
<td>40.5 ± 7.1</td>
</tr>
<tr>
<td>Normotension</td>
<td>696 (69)*</td>
<td>71.0</td>
<td>39.2 ± 6.2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>981</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

Ages are given as mean ± SD.  * number of female

<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>%</th>
<th>Age (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I  Progressed to hypertension</td>
<td>34 (1)**</td>
<td>19.0</td>
<td>42.6±6.7</td>
</tr>
<tr>
<td>II Fluctuation between hypertension and borderline hypertension</td>
<td>49 (3)**</td>
<td>27.4</td>
<td>40.5±6.6</td>
</tr>
<tr>
<td>III Remaining unchanged</td>
<td>35 (3)**</td>
<td>19.6</td>
<td>38.7±6.7</td>
</tr>
<tr>
<td>IV Fluctuation between borderline hypertension and normotension</td>
<td>41 (2)**</td>
<td>22.9</td>
<td>39.8±7.6</td>
</tr>
<tr>
<td>V  Improved to normotension</td>
<td>20 (3)**</td>
<td>11.2</td>
<td>41.4±7.1</td>
</tr>
</tbody>
</table>

H = hypertension,  B = borderline hypertension,  N = normotension,  
* age at the beginning of the study,  ** number of female

Fig.1. Change of blood pressure in borderline hypertensives.

characterized as a condition in which a subject's blood pressure is above the normal range, but the readings are neither sufficiently high to warrant immediate attention nor are they in a clearly hypertensive range. It has been reported that in patients with borderline hypertension, a development into established hypertension later occurred more commonly than in normotensive populations, and that the mortality in patients with borderline hypertension substantially exceeds that observed in normotensive subjects. However, there have been relatively few follow-up studies on borderline hypertension. Thus, the change in blood pressure readings and cardiovascular complications during long observation periods in the borderline hypertensives need to be assessed. This study was designed to analyze changes of blood pressure in a Japanese urban population with borderline hypertension during a 10-year period, and to investigate the relationship between these changes and the risk factors responsible for the development of established hypertension as well as those for cardiovascular complications.

SUBJECTS AND METHODS

The subjects examined were national public service personnel in the Osaka district. Nine hundred and eighty-one subjects (886 males and 95 females, ranging in age from 17 to 55 years), whose blood pressure could be measured 4 times or more a year were included. Casual blood pressure in sitting position was measured using a mercury manometer (Riva-Rocci type) and the highest reading during the year was used. According to the WHO recommendations, systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥95 mmHg were defined as hypertension, blood pressure < 140/90 mmHg as normotension and the remainder as borderline hypertension. Subjects who were diagnosed as

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Fig. 2. The relationship between changes in blood pressure and age in the initial year of this study in borderline hypertensives.

**TABLE II THE MEAN LEVELS OF BLOOD PRESSURE IN THE INITIAL YEAR OF THIS STUDY**

<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>Systolic BP (mmHg)</th>
<th>Diastolic BP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>34</td>
<td>144.8 ± 6.2</td>
<td>89.8 ± 3.4</td>
</tr>
<tr>
<td>II</td>
<td>49</td>
<td>144.6 ± 7.9</td>
<td>88.6 ± 5.0</td>
</tr>
<tr>
<td>III</td>
<td>35</td>
<td>143.9 ± 9.0</td>
<td>84.8 ± 8.6* **</td>
</tr>
<tr>
<td>IV</td>
<td>41</td>
<td>141.5 ± 8.0</td>
<td>85.9 ± 6.0* **</td>
</tr>
<tr>
<td>V</td>
<td>20</td>
<td>141.2 ± 11.4</td>
<td>82.8 ± 9.9* **</td>
</tr>
</tbody>
</table>

(mean ± SD) * p < 0.01 in comparison with group I; ** p < 0.05 in comparison with group II

borderline hypertension in the initial year were followed for more than 10 years. During this period, subjects were given advice about the importance of salt restriction, weight control and exercise, but no antihypertensive drugs were given.

The relationship between the change in blood pressure over 10 years and the clinical features in the initial year was investigated. Four hundred and ninety subjects who remained normotensive during this period were used as controls. The ideal weight was calculated from the following formula: ideal weight (kg) = [height (cm) − 100] × 0.9. Diagnosis of obesity was made when subjects were at least 20% above their ideal weight. Subjects with postprandial glycosuria were given the standard 50g oral glucose tolerance test (GTT) which was assessed by the criteria recommended by the Committee of the Japan Diabetes Society. The family history of hypertension of their father and/or mother was obtained by a questionnaire.

After 10 years electrocardiography (ECG) and ophthalmoscopy were performed. Abnormal ECG findings were taken as one or more of the following Minnesota code items: Q/QS waves, ST depression, T wave inversion or flattening and left ventricular hypertrophy. The hypertensive and/or arteriosclerotic changes of the optic fundi were evaluated by the classification of Scheie. Statistical analysis were performed according to Student's t-test.

**RESULTS**

The Incidence of Normotension, Borderline Hypertension and Hypertension: In 1971, when this study began, the number of hypertensives,
borderline hypertensives and normotensives were 106 (10.8%), 179 (18.2%) and 696 (71.0%), respectively, as shown in Table I. There were no significant age differences among these groups.

Changes of Blood Pressure in Borderline Hypertensives: One hundred and seventy-nine borderline hypertensives in the initial year were classified into the following 5 groups according to the changes in their blood pressure as shown in Fig. 1: the group developing hypertension (group I), the group fluctuating between hypertension and borderline hypertension (group II), the group remaining with borderline hypertension (group
III), the group fluctuating between borderline hypertension and normotension (group IV) and the group improving to normotension (group V). The percentages of each group in the present study were 19.0%, 27.4%, 19.6%, 22.9% and 11.2%, respectively. However, the percentage of normotensive subjects who developed hypertension was only 2.4% (17 out of 696 subjects).

The Relationship between Changes in Blood Pressure and Age in the Initial Year in the Borderline Hypertensives: The group I patients were 14.9, 16.9 and 44.4% in the fourth, fifth and sixth decades of the borderline hypertensives, respectively, while the incidence of borderline hypertensives with a favorable course, i.e., groups III, IV and V, was one half or more in the fourth and fifth decades, but only 33.4% in the sixth decade. Only one subject of group I was among the 5 borderline hypertensives under 30 years old (Fig. 2).

The Mean Levels of Blood Pressure in the Initial Year: Table II shows the mean levels of systolic and diastolic blood pressures in the 5 groups. Although there were no significant differences in systolic blood pressure among the 5 groups, diastolic blood pressures were higher in group I (89.8±3.4 mmHg) and group II (88.6±5.0 mmHg) than those in groups III (84.8±8.6 mmHg), IV (85.9±6.0 mmHg) and V (82.8±8.9 mmHg).

Heart Rate in the Initial Year: The borderline hypertensives showed a significantly higher heart rate (72.9±9.8/min) in the initial year as compared to normotensives (69.2±9.4/min, p < 0.05). No significant differences in heart rate were observed in the 5 groups with borderline hypertension (Fig. 3).

Family History of Hypertension: Figure 4 (a) shows the family history of hypertension. The incidence of the family history in each borderline hypertensive group, except group IV, was higher than in the normotensive group (24.0%). An especially high incidence was observed in groups I (53.8%), II (59.6%) and III (62.5%), respectively. Furthermore, the incidence of subjects whose parents were both hypertensive was significantly higher in groups I, II and III, 12.5, 14.9 and 15.6%, respectively, as compared to 2.1% in the normotensive group. Figure 4 (b) shows the frequency for group I in the borderline hypertensives with or without a family history of hypertension, 17.1 and 15.0%, respectively.

The Incidence of Obesity in the Initial Year: The incidence of obesity in group I (38.2%), that is, the group developing hypertension, was significantly higher as compared to 18.4, 11.4, 2.4, 5.0 and 4.9% in groups II, III, IV and N, respectively (Fig. 5). Obese subjects in group I showed no significant weight reduction for 10 years.

The Incidence of Glucose Intolerance over 10 Years in Each Group: Postprandial glycosuria.
Observation Period in Subjects with Glucose Intolerance and/or Obesity: Hypertension developed in 71.4% of subjects with both obesity and a diabetic GTT curve, in 38.4% of the non-obese subjects with a diabetic GTT and in 35.3% of the obese subjects with a normal GTT. However, it occurred in only 9.2% of the non-obese subjects with normal GTT (Fig. 7).

The Incidence of Electrocardiographic Abnormalities: The incidence of electrocardiographic abnormalities after the 10-year observation period was 32.1, 29.3 and 26.7% in groups I, II and III, respectively, which were all significantly higher than the 11.8% in group N (Fig. 8). Among the abnormal ECG findings, left ventricular hypertrophy was found most frequently in all groups and ST-T changes reflecting ischemia were often found in groups I and II (Table III). Atrial fibrillation was found in one case of group II.

Changes in Ocular Fundi after the 10-year Observation Period: Table IV shows the incidence of arteriosclerotic and/or hypertensive changes in ocular fundi after 10 years. The incidence was higher in groups I (70.0%) and II (57.1%) than in group N (21.4%).

DISCUSSION

Various diagnostic criteria for the so-called borderline hypertension have been used in previous reports. The WHO has defined borderline hypertension as a systolic blood pressure of 140 to 159 mmHg and/or diastolic blood pressure of 90 to 94 mmHg. Julius et al⁷, however, have defined borderline hypertension as a blood pressure intermittently above 150 mmHg in systole or 90 mmHg in diastole. Prior to discussing risk factors for the development of established hypertension, it should be remembered that the individual blood pressure readings fluctuate widely. However, several prospective studies have shown that even a single casual blood pressure has a good long-term prognostic significance. Thus, in the present study borderline hypertension was defined as follows: those subjects, whose highest blood pressure reading in 4 measurements during each year were 140 to 159 mmHg in systole and/or 90 to 94 mmHg in diastole, were diagnosed as borderline hypertensives.

It is interesting to follow the clinical course of borderline hypertension. Although the incidence

The Incidence of Hypertension during the
of established hypertension in borderline hypertensives has often been reported to be higher than in normotensives, different results ranging from 5 to 30% have been reported, which may be explained by differences in the diagnostic criteria of borderline hypertension used, the age of selected subjects and the period of observation, etc. In the present follow-up study of over 10 years, 19.0% of the borderline hypertensives developed hypertension, in contrast to only 2.4% of the normotensives. It has also been reported that an improvement to normotension was not uncommon in some borderline hypertensives. Miyahara has shown that 43% of borderline hypertensives had a normal blood pressure 5 years later. We found that only 11.2% of borderline hypertensives showed an improvement to normotension after 10 years, and 42.5% of these belonged to the group who remained borderline hypertensives or fluctuated between borderline hypertension and normotension. Although it is generally accepted that established hypertension occurs more frequently in borderline hypertensives than in normotensives, it is unreasonable to conclude that borderline hypertension is always the early stage of established hypertension. Therefore, other factors responsible for the development of hypertension were also investigated in borderline hypertensives. The incidence of hypertension was higher in the sixth decade (44.4% of the borderline hypertensives) than in the fourth (14.9%) and fifth decades (16.9%). The incidence of hypertension in borderline hypertensives seemed to increase with age. The initial blood pressure is an important predictive factor for future hypertension. Although this study showed significantly high diastolic pressure in the initial year in the group developing hypertension as compared to the other groups, no significant differences in systolic pressure were found among the 5 groups, suggesting that the diastolic pressure is important as a predictive factor for future hypertension. However, Hedstrand et al concluded in a 3-year follow-up study of borderline hypertensives that the group developing hypertension showed higher systolic pressure than the group remaining unchanged, and that no difference in diastolic pressure was observed between them.

It is generally accepted that most borderline hypertensives...
hypertensives have a hyperkinetic circulation with an increase in heart rate and cardiac output. There have been several reports that the increased resting heart rate might be a predictor for future hypertension.\textsuperscript{7,8} We found no difference in heart rates between the group developing hypertension and the other groups. Hedstrand et al\textsuperscript{15} have also pointed out that the heart rate was not an important risk factor for the development of established hypertension, although Eich et al\textsuperscript{16} suggested that borderline hypertensives with an increased cardiac output showed a better prognosis. Therefore, it is somewhat doubtful whether or not an increased heart rate is important in the development of hypertension.

Thomas et al\textsuperscript{17} and Hedstrand et al\textsuperscript{15} have reported that borderline hypertensives with a family history of hypertension had a higher incidence of established hypertension. We were unable to assess the role of inheritance as a predictor for future hypertension. The precise role of obesity in the pathogenesis of hypertension is still unknown, but there have been many reports stating that obesity may be a risk factor\textsuperscript{18,19} in our study obese subjects were found more frequently in the group developing hypertension from borderline hypertension as shown in Fig. 5. Nearly 30\% of the patients in the group developing hypertension from borderline hypertension showed glucose intolerance. These results suggest that glucose intolerance as well as obesity may be a risk factor. Glucose intolerance, however, is frequently observed in obese subjects. Approximately 70\% of the subjects with both obesity and glucose intolerance developed hypertension as compared to 38.4\% of the non-obese subjects with glucose intolerance and 35.3\% of obese subjects without glucose intolerance, but this occurred in only 9.2\% of those without obesity and glucose intolerance. The coexistence of glucose intolerance and obesity may be a greater predictor for future hypertension than either of them. The possible relation of glucose intolerance to the onset and/or to the development of hypertension remains to be elucidated. With regard to the association of hypertension and diabetes mellitus, Christlieb\textsuperscript{20} has described several possibilities, including the accidental combination of diabetes mellitus to essential hypertension, atherosclerotic hypertension or hypertension due to the development of diabetic nephropathy. Yamori et al\textsuperscript{21} noticed that higher blood sugar concentrations were found more frequently in spontaneously hypertensive rats (SHR) than in normotensive rats, and that glucose intolerance was found before the elevation of blood pressure. They offered an interesting conclusion that the manifestation of hypertension in SHR might be induced by glucose intolerance, or that hypertension and glucose intolerance can result from the same genetic factor. It is well known that abnormalities of lipid metabolism are often observed in patients with diabetes mellitus. The development of established hypertension in borderline hypertensives with glucose intolerance may be partially attributed to increased atherogeneity related to abnormal lipid metabolism.

Many previous surveys have shown that in patients with borderline hypertension a high cardiovascular morbidity and/or mortality appeared to be related to the future development of established hypertension\textsuperscript{22,23} The incidence of ECG abnormalities after 10 years was more than 20\% in all 5 groups with borderline hypertension. It was significantly higher as compared to the normotensive group during the same period. On the contrary, Ishizawa et al\textsuperscript{24} have shown that no borderline hypertensives had left ventricular hypertrophy (LVH) after 10 years. This may be explained by the differences of the ECG criteria used. Their data was based on the definitive LVH criteria established by Kannel et al\textsuperscript{25} while we used the voltage criteria of the Minnesota code. It has been recently reported that the echocardiography has shown myocardial hypertrophy in mild hypertensive patients with a high voltage on electrocardiograms\textsuperscript{26,27} After 10 years, hypertensive and/or arteriosclerotic retinal changes were frequently observed in borderline hypertensives, particularly in the group developing hypertension. Higher incidence of these retinal changes in the group developing hypertension may be in part due to the fact that subjects over 50 years of age were common in this group. However, no coronary occlusions and/or cerebral vascular accidents were observed in the borderline hypertensives.

In conclusion, we suggest that a high diastolic blood pressures in the initial year, a positive family history of hypertension, obesity and glucose intolerance are important risk factors in the development of established hypertension. Therefore, in subjects with borderline hypertension, continuous medical management including correction of obesity as well as glucose intolerance is necessary to prevent the development of established hypertension and its cardiovascular
complications.

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