10-YEAR FOLLOW-UP OF YOUNG MALE PATIENTS WITH MILD HYPERTENSION

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In 1977, 92 male patients with mild hypertension (persistent diastolic blood pressure between 90 and 104 mmHg) were found from among 1608 men aged between 18 and 40 years old who were employees of an industrial company. Of these, 81 patients were followed-up for 10 years. After that time, blood pressures (BP) of 44.4% of the mild hypertensive patients became normotensive (group N); BP of 22.2% remained mild hypertensive (group M); and BP of 33.4% increased to higher levels than the starting BP (group H). Higher levels of systolic and diastolic BP, a higher incidence of family history of hypertension, a higher voltage of SV₁+RV₅ on ECG and a lower concentration of serum triglycerides at the starting point were risk factors for the progression to higher levels of hypertension. Body weights of patients in group H increased significantly during the follow-up period. These results indicate that male mild hypertensive patients with the above-mentioned risk factors should be followed carefully, especially with regard to increased body weights.

HYPERTENSION is a major risk factor for cardiovascular diseases. Treatment of hypertension has been demonstrated to reduce cardiovascular morbidity and mortality even in mild hypertension¹–³. Mild hypertension in adults is defined as a diastolic blood pressure persistently between 90 and 104 mmHg⁴. The natural history of mild hypertension has not yet clearly been determined because of differences in age, sex and follow-up period between studies¹,²,⁵.

The aims of this study were to follow the natural course of mild hypertension and to evaluate the risk factors for the progression of hypertensive disease.

SUBJECTS AND METHODS
One thousand six hundred eight men aged between 18 and 40 years old were selected out of 2325 men who visited the Clinic of Taio Paper MFG., LTD. for their annual medical examination in 1977. The distribution of their ages is shown in Table I.

Blood pressure (BP) was measured in the seated position after at least 10 min of quiet rest using a mercury sphygmomanometer and the lower diastolic BP (DBP) of the two consecutive readings was used. If DBP of 90 mmHg or higher was recorded, BP was measured 2 to 4 times during the next 6 months and the lowest DBP was used as the starting BP. Ninety two subjects were diagnosed having mild hypertension and their BP was followed in the birthday month for 10 years. During this period, the patients were advised repeatedly about the importance of weight control, salt restriction and reduced alcohol consumption. Antihypertensive drugs were administered when systolic BP (SBP) was more than 180 mmHg and/or DBP more than 105 mmHg. Secondary hypertension was ruled out by conventional routine diagnostic tests. Ninety

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two age, height and weight matched controls were randomly selected from the subjects with normal BP. Heart rate was measured for 30 seconds. Height was measured without shoes and body weight was measured with light clothing and 1.0 kg was subtracted from the total weight. An ideal body weight was calculated from the formula: ideal body weight(kg)=[height(cm)-100]×0.9. Obesity index was defined as ratio of body weight to ideal body weight. A family history of hypertension (FHH) in grandparents and/or parents and/or siblings and habits of drinking and smoking were obtained by questionnaire every year. If at least one parent and/or two grandparents were hypertensives, the subject was considered to have a FHH, whereas if none of them were hypertensives, he was considered not to have a FHH. Others were excluded from the analysis of FHH.

Renin releasing test was carried out in 40 of 92 mild hypertensive patients in 1977. After 30 min rest in bed, the blood was taken and 20 mg of furosemide was injected intravenously. The subject was asked to walk in the clinic for 2 hours and then the blood was taken again. Plasma renin activity (PRA) was measured by the method described previously.

Data are expressed as mean ± SD. Statistical analyses of the data were performed with one way analysis of variance and Student's t test. Statistical analyses of family history, habits of drinking and smoking were performed using Bonferroni's methods, and Wilcoxon's T test was used for the statistical analysis of the change of body weight.

**RESULTS**

1. Distribution of BP of 1608 men

Distribution of BP of 1608 men aged between 18 and 40 years old in 1977 is shown in Fig. 1. Ninety two subjects were mild hypertensive patients. Two were patients with isolated systolic hypertension. Twelve were patients with moderate or severe hypertension. Nine of them had been already treated with antihypertensive drugs.

2. Characteristics of mild hypertensive patients at the starting year

As shown in Table 2, the mild hypertensive patients showed significantly higher age, higher higher SBP and DBP, heavier body weight and higher obesity index than the subjects with normal BP.

![Histogram of Systolic BP and Diastolic BP](image)

*Fig.1. Distribution of Systolic and Diastolic Blood Pressures of Subjects Studied in 1977. N=number; BP=blood pressure*

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### TABLE II CLINICAL FEATURES OF SUBJECTS STUDIED

<table>
<thead>
<tr>
<th>Subjects</th>
<th>N</th>
<th>Age (Years)</th>
<th>SBP (mmHg)</th>
<th>DBP (mmHg)</th>
<th>Height (cm)</th>
<th>Body Weight (kg)</th>
<th>Obesity Index (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Blood Pressure</td>
<td>1477</td>
<td>30.6 ± 6.2</td>
<td>113.9 ± 9.2</td>
<td>70.8 ± 7.9</td>
<td>166.5 ± 5.6</td>
<td>59.5 ± 7.2</td>
<td>99.8 ± 11.4</td>
</tr>
<tr>
<td>Borderline Isolated Systolic HT</td>
<td>16</td>
<td>28.4 ± 6.4</td>
<td>143.5 ± 3.2</td>
<td>75.9 ± 6.3</td>
<td>168.7 ± 6.1</td>
<td>64.8 ± 7.7*</td>
<td>105.0 ± 10.7*</td>
</tr>
<tr>
<td>Isolated Systolic HT</td>
<td>2</td>
<td>25.5</td>
<td>166.0</td>
<td>75.0</td>
<td>171.3</td>
<td>63.0</td>
<td>98.2</td>
</tr>
<tr>
<td>Mild HT</td>
<td>92</td>
<td>34.9 ± 5.2*</td>
<td>136.5 ± 11.3</td>
<td>94.9 ± 4.8</td>
<td>165.6 ± 5.4</td>
<td>63.8 ± 9.1*</td>
<td>108.0 ± 12.5*</td>
</tr>
<tr>
<td>Moderate HT</td>
<td>6</td>
<td>35.2 ± 4.8*</td>
<td>154.8 ± 12.4</td>
<td>108.7 ± 2.4</td>
<td>161.8 ± 6.5</td>
<td>62.9 ± 8.6*</td>
<td>113.6 ± 14.4**</td>
</tr>
<tr>
<td>Severe HT</td>
<td>5</td>
<td>34.4 ± 5.5</td>
<td>171.6 ± 11.4</td>
<td>118.0 ± 2.0</td>
<td>164.2 ± 8.6</td>
<td>68.0 ± 19.5*</td>
<td>117.3 ± 30.1</td>
</tr>
<tr>
<td>HT taking Drugs</td>
<td>9</td>
<td>38.0 ± 2.6*</td>
<td>151.6 ± 10.9</td>
<td>100.2 ± 10.0</td>
<td>166.6 ± 3.0</td>
<td>67.3 ± 10.7**</td>
<td>112.7 ± 17.4**</td>
</tr>
</tbody>
</table>

**p < 0.05; *p < 0.01
N = number; SBP = systolic blood pressure; DBP = diastolic blood pressure

### TABLE III CHARACTERISTICS OF CONTROL SUBJECTS AND MILD HYPERTENSIVE PATIENTS

<table>
<thead>
<tr>
<th>N</th>
<th>Age (years)</th>
<th>SBP (mmHg)</th>
<th>DBP (mmHg)</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
<th>FHH (+)</th>
<th>Drinking (+)</th>
<th>Smoking (+)</th>
<th>ECG (HR BPM)</th>
<th>SVt. +RVt. (mV)</th>
<th>SVt. +RVt. (mV)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>92</td>
<td>34.9 ± 5.2</td>
<td>116.7 ± 9.1</td>
<td>73.6 ± 7.7</td>
<td>165.1 ± 5.3</td>
<td>63.2 ± 6.4</td>
<td>60</td>
<td>20</td>
<td>31</td>
<td>61</td>
<td>25</td>
</tr>
<tr>
<td>Mild HT</td>
<td>92</td>
<td>34.9 ± 5.2</td>
<td>136.5 ± 11.3</td>
<td>94.9 ± 4.8*</td>
<td>165.6 ± 5.4</td>
<td>63.8 ± 9.1</td>
<td>41*</td>
<td>43*</td>
<td>31</td>
<td>61</td>
<td>33</td>
</tr>
</tbody>
</table>

### TABLE IV

<table>
<thead>
<tr>
<th>RBC (10⁶/mm³)</th>
<th>Hb (g/dl)</th>
<th>Hct (%)</th>
<th>Uric A (mg/dl)</th>
<th>BUN (mg/dl)</th>
<th>FBS (mg/dl)</th>
<th>TC (mg/dl)</th>
<th>TG (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>498.9 ± 35.9</td>
<td>16.0 ± 1.1</td>
<td>45.8 ± 3.3</td>
<td>5.6 ± 1.3</td>
<td>13.4 ± 2.9</td>
<td>96.5 ± 9.3</td>
<td>195.8 ± 33.5</td>
</tr>
<tr>
<td>Mild HT</td>
<td>498.6 ± 35.5</td>
<td>16.0 ± 1.1</td>
<td>46.1 ± 3.3</td>
<td>6.0 ± 1.1*</td>
<td>13.0 ± 3.4</td>
<td>99.2 ± 12.2</td>
<td>212.6 ± 38.4*</td>
</tr>
</tbody>
</table>

*p < 0.01
FHH = family history of hypertension; HR = heart rate; BPM = beats per minute; RBC = red blood cells; Hb = hemoglobin; Hct = hematocrit; Uric A = uric acid; BUN = blood urea nitrogen; FBS = fasting blood sugar; TC = total cholesterol; TG = triglycerides
3. Comparison of clinical characteristics between the mild hypertensive patients and the control subjects

In order to exclude the influence of age, height and body weight, we compared the clinical characteristics between the mild hypertensive patients and control subjects (Table III). A significantly higher incidence of FHH was observed in the mild hypertensive patients compared with the control subjects, but there was no difference in drinking and smoking habits between the two groups. In laboratory findings, serum concentrations of uric acid, total cholesterol and triglycerides were significantly higher in the mild hypertensive patients than in the control subjects. In ECG findings, heart rates of the mild hypertensive patients were significantly higher than those of the control subjects. There was no difference in voltage of $SV_1 + RV_5$ or $SV_1 + RV_6$ between the two groups.

4. Clinical course of mild hypertension during 10-year follow-up

One patient died of cerebral bleeding and 10 others dropped out because of a change in work place. The remaining 81 patients were followed-up for 10 years.

Table IV shows the clinical course of mild hypertensive patients during 10 years and Table 5 shows BP of the mild hypertensive patients and the control subjects in 1987. During 10-year follow-up 36 mild hypertensive patients became normotensive and 27 patients developed moderate or severe hypertension, while 15% of the normal control developed hypertension in this period.

5. Comparison of the clinical characteristics among 3 groups of mild hypertensive patients at the starting year

Mild hypertensive patients in 1977 were subgrouped according to BP measured in 1987: group N, mild hypertension turned to be normal; group M, continued mild hypertension; group H, mild hypertension to moderate hypertension or hypertension which was treated with antihypertensive drugs. There were no differences in age, height and body weight among the 3 groups as shown in Table 6. However, both SBP and DBP of group H were significantly higher than those of other 2 groups. The incidence of FHH was significantly higher in group H than in group N. Concerning biochemical parameters, the serum concentration of triglycerides in group H was significantly lower than those in other 2 groups. The voltage of $SV_1 + RV_5$ on ECG in group H was significantly higher than those in other 2 groups. The result of renin releasing test is shown in Fig. 2 and in Table 7. PRAs before and after furosemide injection and 2-hour standing were significantly lower in group H than those in other 2 groups.

6. Changes of body weight among 3 groups over 10 years

<table>
<thead>
<tr>
<th>Starting Year</th>
<th>2 Years</th>
<th>4 Years</th>
<th>6 Years</th>
<th>10 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Blood Pressure</td>
<td>0</td>
<td>28 (31.8%)</td>
<td>20 (23.5%)</td>
<td>34 (41.0%)</td>
</tr>
<tr>
<td>Mild Hypertension</td>
<td>92 (100%)</td>
<td>44 (50.0%)</td>
<td>44 (51.8%)</td>
<td>26 (31.3%)</td>
</tr>
<tr>
<td>Moderate HT and HT taking Drugs</td>
<td>0</td>
<td>16 (18.2%)</td>
<td>21 (24.7%)</td>
<td>23 (27.7%)</td>
</tr>
</tbody>
</table>

Total | 92 (100%) | 88 (100%) | 85 (100%) | 83 (100%) | 81 (100%) |

Dropped out | 4 | 7 | 9 | 11 |

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During a 10-year period, there was a tendency for change of body weight of mild hypertensive patients to correlate with change in mean BP (0.05 < p < 0.1).

Fig. 3 shows the change of body weight in each group over the 10 years. In 1987 the body weight of group H was significantly higher than that in 1977. There was no significant change of body weight in groups N and M.

**DISCUSSION**

Follow-up studies on mild hypertension have been reported. However, the definition of mild hypertension, the age of study patients and the period of follow-up were not standardized, so the results are not necessarily comparable. We used the 1986 guidelines of WHO/ISH for the definition of mild hypertension. The follow-up patients in our study were young at the starting point. Since all subjects were working in the same company and living in the same city or neighboring towns, we could exclude the effect of main environmental factors from the study results.

In this study, the body weight of mild hypertensive patients was greater than that of the subjects with normal BP (Table II). Many reports show the relationship between blood pressure and obesity. We compared the characteristics of the mild hypertensive patients with age, height and body weight matched control subjects with normal BP to
exclude the influence of obesity. The characteristics of the mild hypertensive patients were summarized as follows: a higher incidence of FHH, a higher heart rate and higher concentrations of serum uric acid, total cholesterol and triglycerides. A higher heart rate in mild hypertension suggests an activated sympathetic nervous system in these subjects. The outcome of 10-year follow-up of mild hypertension was similar to that reported by Kubo.

The characteristics of the mild hypertensive patients who developed moderate or severe hypertension (group H) were compared with those of the patients in the other 2 groups at the starting point. SBP and DBP of the patients in group H were higher than those of the patients in the other 2 groups. A significantly higher voltage of SV1 + RV5 on ECG in group H was observed. Although the duration of hypertension in group H was unknown, the organ damage might be more advanced compared with the other 2 groups. The results of the renin releasing test supported the assumption that PRA values would decrease as hypertension progressed.11

The serum concentration of triglycerides in group H was significantly lower than that in other 2 groups. Holme et al10 suggested that the rate of change of serum triglycerides correlated with the rate of change in blood pressure. We did not compare the serum concentrations of triglycerides between the starting year and the final year because of the probable effects of antihypertensive drugs. Our study suggests that the risks for developing hypertension in mild hypertensive patients were a higher SBP, a higher DBP, and a higher incidence of FHH and a lower serum concentration of triglycerides.

The change in body weight in mild hypertensive patients over 10 years suggests that it is important to control body weight during a long term follow-up, especially for the patients with the above mentioned high risks. We confirmed the report by Holme et al10 that rate of change in body weight correlated with rate of change in blood pressure for a high DBP at entry.

REFERENCES
2. Management Committee of the Australian National Blood Pressure Study: The Australian therapeu-

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