NONINVASIVE EVALUATION OF LEFT VENTRICULAR FUNCTION
BY SYSTOLIC TIME INTERVALS IN
ESSENTIAL HYPERTENSION WITH ANGINA PECTORIS

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In order to clarify the hemodynamic characteristics in essential hypertension
(HT) with angina pectoris (AP), systolic time intervals (STIs) were measured
in 13 normal subjects (N), 23 patients with AP, 43 HT (WHO stage I: 13,
WHO stage II: 23, WHO stage III: 7) and 19 HT with AP (WHO I: 9, WHO
II: 10).

The ET/PEP ratio was 2.41 ± 0.24 in N, 2.70 ± 0.34 in AP (p < 0.02, vs N),
2.25 ± 0.29 in WHO I, 2.13 ± 0.25 in WHO II (p < 0.01, vs N), 1.54 ± 0.37 in
WHO III (p < 0.001, vs N), 2.68 ± 0.32 in WHO I with AP (p < 0.05, vs N:
p < 0.005, vs HT) and 2.71 ± 0.30 in WHO II with AP (p < 0.02, vs N: p <
0.001, vs HT). Ejection time index (ETI) was 385 ± 15 msec in N, 399 ± 16
in AP (p < 0.05, vs N), 387 ± 13 in WHO I, 385 ± 15 in WHO II, 363 ± 25 in
WHO III (p < 0.05, vs N), 393 ± 16 in WHO I with AP and 402 ± 15 in WHO
II with AP (p < 0.05, vs N: p < 0.01, vs HT). Pre-ejection period index
(PEPI) was 142 ± 10 msec in N, 135 ± 11 in AP, 148 ± 12 in WHO I, 156 ±
13 in WHO II (p < 0.005, vs N), 192 ± 24 in WHO III (p < 0.001, vs N),
134 ± 13 in WHO I with AP (p < 0.05, vs HT) and 136 ± 9 in WHO II with
AP (p < 0.001, vs HT). These results showed that the ET/PEP ratio in HT
with AP was significantly higher than that in HT alone, and this increase in
ET/PEP ratio was mainly due to the shortening of PEP interval in WHO
stage I and the lengthening of ET in addition to it in WHO stage II.

Thus, the changes of STIs in essential hypertension with angina pectoris
are not similar to those in essential hypertension, but identical with those in
patients with angina pectoris.

It is generally considered that elevated levels of
blood pressure play an important role in the
pathogenesis of atherosclerotic disease, the most
prominent cause of mortality. Prospective
studies have convincingly demonstrated that the
development of coronary artery disease is pro-
portional to the degree of elevation of blood
pressure level.¹³

A comparison of hypertensive patients with
and without coronary artery disease revealed a
significant difference in the prognosis.⁴⁵ App-
arently, hypertension not only predisposes
attacks of coronary artery disease, but once such
attack occurs, is more likely to cause them to be fatal.⁶ Also, the increased load imposed by the

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hypertension may intensify the degree of ischemia of the myocardium.

The mortality rate is reduced by antihypertensive therapy, but death from coronary artery disease remains a major problem.7-9

Thus, the presence of coronary artery disease is one of the most important factors in determining the prognosis of hypertensive patients, and attention is directed to the early detection and treatment of coexistent coronary artery disease.

Analysis of systolic time intervals is one of the most widely practiced noninvasive methods to evaluate the cardiac function in patients with hypertension and coronary artery disease.10-16 However, there is almost no report on the noninvasive evaluation of cardiac function in hypertensive patients with coronary artery disease.

We previously reported that analysis of systolic time intervals was useful to evaluate the left ventricular function in patients with coronary artery disease.17

The purpose of the present report is to evaluate noninvasively the left ventricular function by systolic time intervals in hypertensive patients with angina pectoris.

MATERIALS AND METHODS

Patients

Patients were divided into four groups:

Group A:

This group consisted of 19 patients with essential hypertension (thirteen men and six women) who had a history of angina pectoris.

Group B:

This group consisted of 43 patients with essential hypertension (thirty-four men and nine women), selected in order to match the patients in Group A as closely as possible regarding age. None of them had a history of angina pectoris or myocardial infarction.

All patients of Group A and Group B were subdivided into the three groups of stage I, stage II and stage III, according to the WHO classification.18 The group of WHO stage III consisted of patients who had a history of heart failure.

Group C:

This group consisted of 23 patients with angina pectoris (seventeen men and six women) but no history of hypertension. They were matched according to age with Group A.

Angina pectoris was diagnosed when substernal distress of brief duration, brought on by exercise and relieved by rest or nitroglycerin, was present. All patients of Group A and Group C had a significant narrowing in coronary artery (narrowing of the luminal diameters greater than 75%) demonstrated by coronary arteriography.

Group D:

Thirteen normotensive subjects who underwent cardiac catheterization for further examination of chest pain and revealed no significant narrowing in coronary artery and had normal ejection fraction were selected as normal control. They were matched according to age with the other three patient groups.

All patients of the four groups had regular sinus rhythm with normal A-V conduction with no bundle branch block.

Examination in each group except WHO stage III were carried out under no-treatment condition for at least ten days.

Measurement of Systolic Time Intervals (STIs)

Electrocardiogram, phonocardiogram and carotid pulse tracing were simultaneously recorded using a MIC-8800 polygraph (Fukuda Denshi Co., Ltd.) at a paper speed of 100 mm per second. Phonocardiogram was recorded using a MA-250 (Fukuda Denshi Co., Ltd.) and carotid pulse tracing was recorded using a TY-303 transducer (Fukuda Denshi Co., Ltd.).

Total electromechanical systole (Q-II time) was measured from the onset of the QRS complex to the first high-frequency vibrations of the aortic component of the second heart sound. Left ventricular ejection time (ET) was measured from the onset of the upstroke of the carotid pulse tracing to the dicrotic notch. Pre-ejection period (PEP) was determined by subtracting ET from Q-II time. The ET and PEP values were corrected for heart rate using Weisler's widely accepted correction formula.19 The ratio of ejection time to pre-ejection period (ET/PEP) was calculated. These intervals were derived by averaging the measurements of 5 consecutive beats. Mean values of STIs were compared among patient groups.

Statistical Analysis

Comparison of the data between the groups was made using Student's t test for unpaired data.

RESULTS

The results (summarized in Table I) demonstrate that there was no significant difference in

<table>
<thead>
<tr>
<th>Group</th>
<th>Clinical Profile</th>
<th>Age (years)</th>
<th>HR (beats/min)</th>
<th>SBP (mmHg)</th>
<th>DBP (mmHg)</th>
<th>ET (msec)</th>
<th>ETI (msec)</th>
<th>PEP (msec)</th>
<th>PEPI (msec)</th>
<th>ET/PEP</th>
</tr>
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<tbody>
<tr>
<td>A</td>
<td>Hypertension with angina pectoris</td>
<td>WHO I</td>
<td>53.2</td>
<td>58.6</td>
<td>133</td>
<td>80</td>
<td>293++</td>
<td>393</td>
<td>111</td>
<td>134*</td>
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<tr>
<td></td>
<td>(n = 9)</td>
<td>± 5.8</td>
<td>± 5.0</td>
<td>± 16</td>
<td>± 6</td>
<td>± 14</td>
<td>± 16</td>
<td>± 12</td>
<td>± 13</td>
<td>± 0.32</td>
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<tr>
<td></td>
<td>WHO II</td>
<td>53.6</td>
<td>60.0</td>
<td>159****</td>
<td>93****</td>
<td>300++</td>
<td>402++</td>
<td>112++++</td>
<td>116++++</td>
<td>136++++</td>
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<td></td>
<td>(n = 10)</td>
<td>± 8.5</td>
<td>± 6.6</td>
<td>± 24</td>
<td>± 11</td>
<td>± 17</td>
<td>± 15</td>
<td>± 10</td>
<td>± 9</td>
<td>± 0.30</td>
</tr>
<tr>
<td>B</td>
<td>Hypertension</td>
<td>WHO I</td>
<td>39.1</td>
<td>69.8</td>
<td>134</td>
<td>81</td>
<td>268</td>
<td>387</td>
<td>120</td>
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<td>± 11.7</td>
<td>± 11.0</td>
<td>± 20</td>
<td>± 9</td>
<td>± 23</td>
<td>± 13</td>
<td>± 12</td>
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<td>WHO II</td>
<td>48.1</td>
<td>61.3</td>
<td>155****</td>
<td>92****</td>
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<td>385</td>
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<td>± 11</td>
<td>± 19</td>
<td>± 15</td>
<td>± 13</td>
<td>± 13</td>
<td>± 0.25</td>
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<tr>
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<td>WHO III</td>
<td>50.3</td>
<td>69.1</td>
<td>177****</td>
<td>98****</td>
<td>246***</td>
<td>363*</td>
<td>164++++</td>
<td>192****</td>
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<td>(n = 7)</td>
<td>± 12.6</td>
<td>± 11.9</td>
<td>± 21</td>
<td>± 8</td>
<td>± 34</td>
<td>± 25</td>
<td>± 24</td>
<td>± 24</td>
<td>± 0.37</td>
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<tr>
<td>C</td>
<td>Angina pectoris</td>
<td>(n = 23)</td>
<td>53.5</td>
<td>57.2</td>
<td>121</td>
<td>79</td>
<td>301*</td>
<td>399*</td>
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<td>± 9.6</td>
<td>± 6.3</td>
<td>± 8</td>
<td>± 4</td>
<td>± 25</td>
<td>± 16</td>
<td>± 11</td>
<td>± 11</td>
<td>± 0.34</td>
<td></td>
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<td>D</td>
<td>Normal subjects</td>
<td>(n = 13)</td>
<td>46.6</td>
<td>62.2</td>
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<td>78</td>
<td>279</td>
<td>385</td>
<td>117</td>
<td>142</td>
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<tr>
<td></td>
<td>± 7.2</td>
<td>± 5.5</td>
<td>± 6</td>
<td>± 4</td>
<td>± 15</td>
<td>± 15</td>
<td>± 12</td>
<td>± 10</td>
<td>± 0.24</td>
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</table>

Values are shown as mean ± SD.
Abbreviations: HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; ET = ejection time; ETI = ejection time index; PEP = pre-ejection period; PEPI = pre-ejection period index.

* = p < 0.05; ** = p < 0.02; *** = p < 0.01; **** = p < 0.005 and ***** = p < 0.001; as compared to normal subjects; + = p < 0.05; ++ = p < 0.01; +++ = p < 0.005 and ++++ = p < 0.001; as compared to hypertensive patients without angina pectoris.
mean heart rates between all patient groups.

Blood pressure was significantly higher in patients of WHO stage II, in both Group A and Group B, than in normal subjects (p < 0.001, p < 0.001, respectively) and than in patients of WHO stage I (p < 0.01, p < 0.01, respectively). There was no significant difference in blood pressure between Group C and Group D, nor between Group A and Group B.

**Systolic Time Intervals**

There were statistically significant differences in the systolic time interval values between hypertensive patients with angina pectoris and hypertensive patients without angina pectoris, as well as between patients with angina pectoris and normal subjects.

The ET/PEP Ratio (Fig. 1): The ET/PEP ratio was significantly greater in Group C than in Group D (p < 0.02). In Group B, the ET/PEP ratio was decreased as the WHO stage developed. The ET/PEP ratio was significantly lower in patients of WHO stage II than in Group D (p < 0.01) and was extremely low in patients of WHO stage III. On the other hand, in Group A, the ET/PEP ratio was significantly higher in patients of both WHO stage I and stage II than in Group D (p < 0.05, p < 0.02, respectively) and Group B (p < 0.005, p < 0.001, respectively). There was no significant difference in ET/PEP ratio between Group A and Group C.

Ejection Time Index (ETI) (Fig. 2): The ETI in Group C was significantly prolonged compared with that in Group D (p < 0.05). There was no significant difference in the ETI between Group B except patients of WHO stage III and Group D. The ETI was extremely shortened in patients of WHO stage III. In Group A, the ETI was significantly prolonged in WHO stage II compared with that in Group B (p < 0.01). There was no significant difference in ETI between Group A and Group C.

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Fig. 3. Comparison of pre-ejection period index between all patient groups.

* = p < 0.005 and ** = p < 0.001, as compared to normal subjects, + = p < 0.05 and ++ = p < 0.001, as compared to hypertensive patients without angina pectoris.

Pre-ejection Period Index (PEPI) (Fig. 3): There was no significant difference in the PEPI between Group C and Group D. In Group B, the PEPI was prolonged as the WHO stage developed. The PEPI was significantly longer in patients of WHO stage II than in Group D (p < 0.005) and was extremely prolonged in patients of WHO stage III. There was a positive correlation between left ventricular mean wall thickness (LVMWT), calculated from echocardiographic measurements as follows; LVMWT = (LV posterior wall thickness + interventricular septal thickness)/2, and PEP (y = 0.180x - 3.2, r = 0.744, p < 0.001). A lower but significant correlation was present between systolic blood pressure and PEP (y = 0.546x + 79, r = 0.540, p < 0.005). There was no significant difference in the PEPI between Group A and Group D or Group C. The PEPI in Group A, in patients of both WHO stage I and stage II, was significantly shortened compared with that in Group B (p < 0.05, p < 0.001, respectively).

**DISCUSSION**

In a previous study, we reported\textsuperscript{17} that the systolic time interval values were actually 'supernormal' in patients with angina pectoris as compared to normal subjects. In the present study, we met with similar results, that is, in patients with angina pectoris the ET/PEP ratio was significantly increased compared with that in normal subjects, and this increase in the ET/PEP ratio was mainly due to the prolongation of ET.

There are many reports\textsuperscript{20–22} on the evaluation of the left ventricular function in hypertension. It should be noted that the results of these studies in both experimental models and hypertensive patients\textsuperscript{23} have been conflicting. In animal studies, the performance in chronic pressure overload has been reported to be depressed\textsuperscript{24} normal\textsuperscript{25} or even 'supernormal'\textsuperscript{26}. Frohlich and co-workers\textsuperscript{20} reported impairment of the left ventricular function in untreated hypertensive patients with left ventricular hypertrophy. Strauer\textsuperscript{27} reported the left ventricular function within the normal range in untreated hypertensive patients. The conflict may be due to the lack of standardized evaluation methods of the left ventricular function. Therefore, we examined the left ventricular function using systolic time intervals, a very sensitive method for the noninvasive evaluation of the left ventricular function. The present data indicate that the left ventricular systolic function in hypertensive patients is depressed by degrees according to the development of hypertension. The ET/PEP ratio in hypertensive patients of WHO stage II was significantly lower than that in normal subjects and this decrease in the ET/PEP ratio was mainly due to the prolongation of PEP. Since a positive correlation between left ventricular mean wall thickness and PEP and a lower but significant correlation between systolic blood pressure and PEP were present, the prolongation of PEP probably reflected the diminution in myocardial contractile performance occurring in the hyper trophyed left ventricle. The increased afterload might, in part, be responsible for it. The decreased ET/PEP ratio in hypertensive patients of WHO stage III was accounted for by both the lengthening of PEP and the shortening of ET. This probably reflected the defect in myocardial contractile performance occurring in the failing left ventricle.

There have been almost no reports on the noninvasive evaluation of the left ventricular
function in hypertensive patients with ischemic heart disease. In the present study, the systolic time interval values in hypertensive patients with angina pectoris were 'supernormal' rather than depressed. The ET/PEP ratio was significantly higher in hypertensive patients with angina pectoris of both WHO stage I and stage II than in hypertensive patients without angina pectoris. Individual values in the two groups showed considerable overlap in WHO stage I, but in WHO stage II when myocardial involvement due to hypertension is clinically overt, there was minimal overlap. This increase in the ET/PEP ratio was caused by the shortening of the PEP interval in patients of WHO stage I and by the simultaneous prolongation of ET and shortening of PEP in patients of WHO stage II. Thus, the changes of systolic time intervals in hypertensive patients with angina pectoris are not similar to those in hypertensive patients without angina pectoris. They are identical with those in patients with angina pectoris. The cause of the prolongation of ET in hypertensive patients with angina pectoris has yet been unclear. Because there was no significant difference in systolic blood pressure and left ventricular end-diastolic dimension measured by echocardiography, between hypertensive patients with angina pectoris and those without angina pectoris, neither the afterload nor preload factor were responsible for both the prolongation of ET and the shortening of PEP in hypertensive patients with angina pectoris. In a previous study, we suggested that the prolongation of ET in patients with angina pectoris might be the consequence of reduced myocardial contractility due to a reduced blood supply through the stenotic coronary artery, while the shortening of PEP in patients with angina pectoris might be caused by the high levels of intrinsic catecholamine. The same mechanism as in patients with angina pectoris may be responsible for the changes of systolic time intervals in hypertensive patients with angina pectoris.

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