Stiffness of Systemic Arteries in Patients With Myocardial Infarction
A Noninvasive Method to Predict Severity of Coronary Atherosclerosis

Tadakazu Hirai, MD, Shigetake Sasayama, MD, Takeshi Kawasaki, MD, and Shin-ichi Yagi, PhD

The static elastic properties of arterial tree (abdominal aorta and common carotid artery) were studied in 19 normal subjects and in 49 patients with myocardial infarction with an ultrasonic phase-locked echo-tracking system that allows continuous transcutaneous measurement of the arterial diameter. The stiffness index \( \beta \), which represented the mechanical properties in the arterial wall, was calculated from the relation between systemic blood pressure and the diameter of the artery. Patients with myocardial infarction underwent coronary angiography in their convalescent period to determine involved vessels. In 11 patients, coronary artery was patent; 15 patients had one-vessel disease, 12 had two-vessel disease, and the remaining 11 patients had three-vessel disease. In normal subjects, increasing age was associated with an increase in arterial stiffness. An average value of the stiffness index of the abdominal aorta was 8.58±3.02 (mean±SD) and that of common carotid artery was 9.17±2.22. In patients with three-vessel disease, these values were significantly higher (22.37±4.29 in abdominal aorta and 13.17±4.56 in common carotid artery) than those in normal subjects. Stiffness index of patients with two- or one-vessel disease was also increased but lower than those in patients with three-vessel disease \((p<0.05)\). Forty-four of 49 patients with infarction had an arterial stiffness index of abdominal aorta higher than the 95% confidence limits of the normal data \((p<0.05)\). Twenty-eight patients were outside the nomogram of common carotid artery \((p<0.05)\). The mechanical properties of these elastic arteries provided sufficiently reliable information on changes caused by atherosclerosis. (Circulation 1989;80:78–86)

The amount of severity of atherosclerosis in the coronary bed shows a positive correlation with the degree of atherosclerosis in the aorta or other major arterial branches.1–5 Atherosclerotic changes in arterial wall have been shown to include smooth muscle cell proliferation, deposition of lipid, and accumulation of collagen, elastin, and proteoglycans.6,7 Changes in the ratio of collagen to elastin have been known to structurally affect the elastic behavior of arterial walls. The former is much stiffer than the latter, the elastic modulus (Young’s modulus) being about \( 1,000 \times 10^6 \) dynes/cm\(^2\) at 100% elongation in collagen and only \( 3 \times 10^6 \) dynes/cm\(^2\) in elastin.8,9 However, conflicting results have been reported in the literature concerning the arterial wall stiffness in atherosclerosis.

Quantitative information on the elastic properties of the large arteries can be obtained by means of concomitant determinations of pressure and arterial diameter. Intensive investigations have been continued to assess the state and function of large arteries noninvasively for early detection of atherosclerotic damage of these vessels.10,11 Functional changes in arterial stiffness have been investigated by pulse wave velocity or by ultrasonically measured pulsatile arterial diameter changes.10–14 However, these measures have inherent limitations for clinical application because of their dependence on arterial pressure or susceptibility of peripheral muscular arteries to the measuring environment.

Recently, we developed an ultrasonic phase-locked echo-tracking system that allows transcutaneous measurement of the arterial caliber and showed that the stiffness indexes can be calculated noninvasively from the relation between systemic blood pressure and arterial diameter.15 In the pres-
ent study, by means of this ultrasonic technique, we determined and compared the distensibility of abdominal aorta and common carotid artery in normal subjects with those in patients with coronary artery disease. A quantitative assessment of arterial damage caused by the process of atherosclerosis will provide better prediction of ischemic heart disease than estimation based solely on traditional coronary risk factors.\textsuperscript{10,16}

**Methods**

**Patient Population**

Over a 2-year period, 49 patients (37 men and 12 women, aged 42–76 years) with a myocardial infarction were referred for coronary angiography during their convalescent period; the distensibility of their arterial walls was also studied. Patients with valvular heart disease or arrhythmia were excluded from this study. The diagnosis of myocardial infarction was based on accepted criteria: central chest pain, shock or syncope suggesting infarction together with typical changes in serum levels of cardiac enzymes, or a pathologic Q wave or localized ST changes on the standard 12-lead electrocardiogram. In each patient, coronary risk factors (including blood chemistry and cigarette smoking habits) were carefully assessed.

**Arterial Distensibility Measurement**

The transverse displacement of the arterial wall was measured with an ultrasonic phase-locked echotracking system, which was equipped with a real-time linear array scanner. The details of this method were described elsewhere.\textsuperscript{15,17,18} Briefly, this technique was based on a phase-locked loop method that enables the zero crossing phase of the echoes reflected from the arterial wall to be tracked. With this technique, the transverse displacements of the arterial wall of the lower abdominal aorta and the right and left carotid arteries were recorded noninvasively. A typical pulsatile arterial wall displacement recorded with the echo track is shown in Figure 1. The central frequency of the ultrasonic probe used in this method was selected to be either 3.5, 5.0, or 7.5 MHz according to the acoustic condition of the individual arteries. Then, brachial arterial pressure was measured by the conventional cuff method, using a linear, wide-band pressure transducer fixed under the cuff (US Patent No. 4144879) (Figure 2). This indirect blood pressure differed by only 4 mm Hg from direct arterial blood pressure.\textsuperscript{15}

Hayashi et al\textsuperscript{19,20} analyzed static behaviors of arterial walls through changes in external radii due to distending pressure. Stress-strain behavior was then determined from their pressure-diameter relation data by using the finite deformation theory. From this analysis and their experimental data, they assumed that a simple exponential relation exists between the relative pressure and the distension ratio.

According to the experimentally obtained relations between the intraluminal pressures and the external radii, they defined the distension ratio (λ) as the arterial diameter (Dx) at a given pressure (Px), normalized by the diameter (Do) at a standard pressure (Po). When the distension ratio was plotted against the logarithmic value of the relative pressure (Px/Po, a given pressure normalized by standard pressure of 100 mm Hg), a linear relation was observed in the physiologic range of pressure. This relation is expressed as:

\[
\ln \frac{P_x}{P_o} = \beta (\lambda - 1) \quad (1)
\]

\[
\ln \frac{P_x}{P_o} = \beta \left( \frac{D_x - D_o}{D_o} \right) \quad (2)
\]

The index \( \beta \) represents the stiffness of the vascular walls. However, because Do at standard pressure (100 mm Hg) cannot be measured clinically, we extrapolated these concepts to the clinical setting by trying to modify Equation 2 in the following manner.

If the artery is assumed to be subject to systolic pressure (Ps) and diastolic pressure (Pd) where the external diameter is Dd at diastole and Ds at systole, Equation 2 can be written as:

\[
\ln P_s - \ln P_o = \beta \left( \frac{D_s - D_o}{D_o} \right) \quad (3)
\]

\[
\ln P_d - \ln P_o = \beta \left( \frac{D_d - D_o}{D_o} \right) \quad (4)
\]

By subtracting Equation 4 from Equation 3, \( \beta \) is then given as:

\[
\beta = \frac{\ln P_s}{P_d} \frac{D_s - D_d}{D_o} \quad (5)
\]
where

\[
\beta = \beta' \left( \frac{D_0}{Dd} \right)
\]

Equation 7 can be rearranged as:

\[
\frac{\beta}{\beta'} = 1 + \left( \frac{D_0 - Dd}{Dd} \right)
\]

Here, we note that changes of diameter during a cardiac cycle do not usually exceed 10% in all arteries of subjects over 20 years of age. In a normotensive subject, the following relations are observed:

\[
\frac{D_0 - Dd}{Dd} < \frac{D_s - Dd}{Dd} < 1
\]

\[
\beta = \beta' = \frac{\ln \frac{P_s}{Pd}}{\frac{D_s - Dd}{Dd}}
\]

Thus, \( \beta \) is approximately equal to \( \beta' \), and so we can calculate from pressure and dimensional data obtained noninvasively.

To compare the stiffness index \( \beta \) with Peterson's pressure modulus, we calculated pressure-strain elastic modulus (\( E_p \)).

\[
E_p = \frac{\Delta P \cdot R}{\Delta R}
\]

where \( \Delta P \) is pulse pressure, \( \Delta R \) is pulsatile radius, and \( R \) is diastolic radius. Instead, we used \( P_s, P_d, D_s, \) and \( D_d \) to give:

\[
E_p = \frac{P_s - P_d}{D_s - Dd} \cdot Dd
\]

To show the independence of the stiffness index from pressure, the arterial stiffness was measured in eight patients with myocardial infarction in whom nitroprusside was administrated intravenously at a rate of 0.5–2.0 \( \mu \)g/kg/min. Systolic and diastolic arterial pressures decreased from 149±6 to 114±8 mm Hg (mean±SD) and from 75±14 to 65±10 mm Hg, respectively. To compare the characteristics of stiffness index \( \beta \) and \( E_p \), each value was normalized by the mean values as shown in Figure 3. The stiffness index was almost constant and not influenced by changes in systolic pressure. On the contrary, \( E_p \) decreased linearly along with the reduction in the arterial systolic pressure. Thus, the stiffness index provides reliable measure of elasticity because it is independent of arterial pressure.

**Coronary Angiography**

Coronary arteriography was performed by the Judkins or Sones techniques. The coronary artery was opacified with 5–8 ml 75% Urografin and taken with 35 mm film at 60 frames/sec. The coro-
Analysis of Data

To interpret the values of the stiffness index of patients with coronary artery disease, we constructed a nomogram to age, which is the critical variable that governs atherosclerotic process. In 39 normal subjects (age, 6–80 years), arterial stiffness indexes \( \beta \) were correlated with age as previously reported.\(^{15}\) The 95% confidence limits of the regression equation for these data allowed a definition of statistical range for the \( \beta \) values of normal subjects, and they were used as age-matched controls. All the subjects were normotensive, and none had cardiac, neurologic, or renal involvement or arteriopathy of the four extremities. There were no abnormal findings on electrocardiogram and chest radiographs or in serum cholesterol and fatty acid concentrations.

Statistical Analysis

All values of stiffness index in each group were averaged and expressed as mean±SD. Analysis of variance with the subsequent Newman-Keuls multiple comparison method was also applied to analyze data. Analysis of difference of proportions was performed with a \( \chi^2 \) test (Fisher’s exact test). The level of significance was \( p<0.05 \).

Results

Risk Factors

A summary of coronary risk factors in the three groups of patients with coronary artery disease is given in Table 1. No statistically significant differences were observed among the three groups in age, total cholesterol, serum triglycerides, and blood pressure; however, blood glucose level and the proportion of smokers were significantly higher in patients with three-vessel disease.

Size of Arterial Diameter

There were no significant changes in arterial pressure among the five groups. In both abdominal
Blood pressure response to cigarette smoking was augmented in subjects with significant epicardial coronary disease compared with the normal control group, and there was no significant difference in blood pressure response to cigarette smoking between patients with one-vessel and two-vessel disease. The beta values determined for the overall group were: 

\[
\beta_{\text{abdominal aorta}} = 0.09 \times \text{age} + 3.2 \\
\beta_{\text{common carotid artery}} = 0.11 \times \text{age} + 2.8
\]

Of 49 patients with myocardial infarction, 28 had a stiffness index \( \beta \) of common carotid arteries higher than the upper 95% confidence limits of the normal data \((p<0.05)\), whereas the 21 remaining patients were inside the nomogram. With regard to abdominal aorta, in 44 patients \( \beta \) values were outside of the nomogram \((p<0.05)\) and in only five

### Table 1. Mean Values for Coronary Risk Factors

<table>
<thead>
<tr>
<th>Patients ((n))</th>
<th>Normal control subjects</th>
<th>No significant coronary stenosis</th>
<th>One-vessel disease</th>
<th>Two-vessel disease</th>
<th>Three-vessel disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>59.9±11.8</td>
<td>54.9±7.2</td>
<td>59.3±10.2</td>
<td>58.5±6.1</td>
<td>56.9±7.0</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dl)</td>
<td>54.7±12.3</td>
<td>40.4±8.5*</td>
<td>44.9±24.6</td>
<td>40.7±9.4</td>
<td>33.6±8.4*</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>165.9±29.5</td>
<td>216.5±99.0</td>
<td>209.7±79.4</td>
<td>226.5±63.0</td>
<td>201.1±48.5</td>
</tr>
<tr>
<td>Serum triglycerides (mg/dl)</td>
<td>144.8±30.4</td>
<td>202.8±256.4</td>
<td>130.7±88.5</td>
<td>118.6±51.8</td>
<td>137.8±67.2</td>
</tr>
<tr>
<td>Systolic pressure (mm Hg)</td>
<td>123.6±16.2</td>
<td>128.0±18.1</td>
<td>132.3±21.8</td>
<td>140.2±27.4</td>
<td>134.0±28.3</td>
</tr>
<tr>
<td>Diastolic pressure (mm Hg)</td>
<td>74.0±10.2</td>
<td>79.3±11.5</td>
<td>79.3±11.0</td>
<td>83.1±13.6</td>
<td>80.9±13.9</td>
</tr>
<tr>
<td>Blood glucose (mg/dl)</td>
<td>86.8±9.8</td>
<td>97.2±16.4</td>
<td>112.8±55.2</td>
<td>115.7±40.5</td>
<td>144.9±84.1*</td>
</tr>
<tr>
<td>Smoking (cigarettes/day)</td>
<td>9.8±6.5</td>
<td>26.8±17.2</td>
<td>19.6±17.1</td>
<td>15.4±15.9</td>
<td>25.5±21.3*</td>
</tr>
</tbody>
</table>

Values are given as mean±SD.
*p<0.05 compared with value for group with normal subjects.

### Table 2. Mean Values of Five Groups for Arterial Dimensional Data and Stiffness Index

<table>
<thead>
<tr>
<th>Abdominal aorta</th>
<th>Normal control subjects</th>
<th>No significant coronary stenosis</th>
<th>One-vessel disease</th>
<th>Two-vessel disease</th>
<th>Three-vessel disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{Ps} ) (mm Hg)</td>
<td>123.3±13.8</td>
<td>123.8±14.0</td>
<td>123.1±10.8</td>
<td>121.2±12.7</td>
<td>130.9±24.3</td>
</tr>
<tr>
<td>( \text{Pd} ) (mm Hg)</td>
<td>72.7±9.6</td>
<td>77.1±9.2</td>
<td>77.2±8.5</td>
<td>74.8±5.8</td>
<td>77.1±9.0</td>
</tr>
<tr>
<td>( \text{Dd} ) (mm)</td>
<td>14.9±4.2</td>
<td>17.6±3.0</td>
<td>19.0±3.4</td>
<td>18.7±4.0</td>
<td>17.6±2.0</td>
</tr>
<tr>
<td>( \text{Ds} - \text{Dd} ) (mm)</td>
<td>0.89±0.21</td>
<td>0.70±0.17</td>
<td>0.64±0.18</td>
<td>0.62±0.30*</td>
<td>0.36±0.13*†‡</td>
</tr>
<tr>
<td>( \text{Ep} \times \text{dynes} \cdot \text{cm}^{-2} \cdot 10^{3} )</td>
<td>1.10±0.31</td>
<td>1.62±0.37</td>
<td>1.78±0.46</td>
<td>2.15±0.70*</td>
<td>3.08±0.99*‡†‡‡</td>
</tr>
<tr>
<td>( \beta )</td>
<td>8.58±3.02</td>
<td>12.25±1.92</td>
<td>14.39±3.62*</td>
<td>16.63±5.15*</td>
<td>22.37±4.29*‡‡‡</td>
</tr>
</tbody>
</table>

Subjects who exceed the nomogram in each group \((n)\)

<table>
<thead>
<tr>
<th>Common carotid artery</th>
<th>Normal control subjects</th>
<th>No significant coronary stenosis</th>
<th>One-vessel disease</th>
<th>Two-vessel disease</th>
<th>Three-vessel disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{Ps} ) (mm Hg)</td>
<td>123.0±15.9</td>
<td>124.4±15.5</td>
<td>122.7±14.3</td>
<td>120.8±16.7</td>
<td>131.2±27.5</td>
</tr>
<tr>
<td>( \text{Pd} ) (mm Hg)</td>
<td>72.5±9.8</td>
<td>76.0±9.4</td>
<td>77.2±8.9</td>
<td>73.2±6.7</td>
<td>75.4±10.1</td>
</tr>
<tr>
<td>( \text{Dd} ) (mm)</td>
<td>7.6±2.1</td>
<td>8.0±1.1</td>
<td>8.4±0.9</td>
<td>8.4±0.9</td>
<td>8.6±0.5</td>
</tr>
<tr>
<td>( \text{Ds} - \text{Dd} ) (mm)</td>
<td>0.45±0.22</td>
<td>0.44±0.15</td>
<td>0.41±0.17</td>
<td>0.43±0.20</td>
<td>0.36±0.13</td>
</tr>
<tr>
<td>( \text{Ep} \times \text{dynes} \cdot \text{cm}^{-2} \cdot 10^{3} )</td>
<td>1.21±0.36</td>
<td>1.23±0.30</td>
<td>1.38±0.35</td>
<td>1.42±0.43</td>
<td>1.84±0.98*‡‡‡</td>
</tr>
<tr>
<td>( \beta )</td>
<td>9.17±2.22</td>
<td>9.42±2.21</td>
<td>10.54±2.04</td>
<td>11.44±3.39*†‡‡‡</td>
<td>13.17±4.56*‡‡‡</td>
</tr>
</tbody>
</table>

Values are given as mean±SD.
Ps, systolic arterial pressure; Pd, diastolic arterial pressure; Dd, arterial diameter at diastole; Ds, arterial diameter at systole; Ep, pressure-strain elastic modulus; \( \beta \), stiffness index.
*p<0.05 vs. the group of normal subjects; †p<0.05 vs. the group of patients with no significant coronary stenosis; ‡p<0.05 vs. the group of patients with one-vessel disease; §§p<0.05 vs. the group of patients with two-vessel disease; ††p<0.05, proportions of patients who exceed the nomogram compared with the normal control subjects.
Arterial Stiffness and Coronary Artery Disease

By Hirai et al.

FIGURE 4. Nomogram of stiffness index in abdominal aorta. Dotted lines indicate the actual regression line; solid lines designate the 95% confidence limits for normal data. Upper panel: normal control subjects; lower panel: myocardial infarction group. Lower panel: n, no significant coronary stenosis (0-VD); ▲, one-vessel disease (1-VD); □, two-vessel disease (2-VD); ○, three-vessel disease (3-VD).

FIGURE 5. Nomogram of stiffness index in common carotid artery. Upper panel: normal control group; lower panel: myocardial infarction group. Lower panel: ●, no significant coronary stenosis (0-VD); ▲, one-vessel disease (1-VD); □, two-vessel disease (2-VD); ○, three-vessel disease (3-VD).

Pressure-Strain Elastic Modulus

Ep in both abdominal aorta and common carotid artery is shown in Figure 7. Ep was increased with the extent of coronary artery disease but only in those with three-vessel disease; values in both arteries reached a statistical significance (p<0.05).

Discussion

In the present study, we observed a decrease in arterial distensibility of abdominal aorta and carotid arteries noninvasively by means of ultrasonic technique in patients with coronary artery disease. The stiffness index β is the slope of the exponential function between the relative arterial pressure and the distention ratio of artery (the arterial diameter at a given pressure).15,19,20 This index characterizes the entire deformation behavior of the vascular wall, being independent of the intraluminal pressure within the physiologic range. Because elasticity of the arterial wall decreases with age, it is necessary to exclude differences related to age. In the previous study,15 we demonstrated the age-related changes in β values of major branches of the human arteries. An increase in stiffness of arteries with advancing age has been related to the structural and

patients did it remain inside. All patients with two- or three-vessel disease, in particular, had the arterial stiffness of abdominal aorta higher than the 95% confidence limits of the normal data (Figure 4). The proportion of abnormal subjects who exceed the nomogram in each group was increased with the extent of coronary artery disease (Table 2).

Arterial Stiffness and Severity of Coronary Artery Disease

In normal subjects, mean values of stiffness index β were essentially the same in abdominal aorta and common carotid arteries; however, in patients with coronary artery disease, these values tended to be higher in the former than the latter in each group (Figure 6).

In both arteries, the β values were highest in patients with three-vessel disease and decreased along with the less severe coronary involvement, being lowest and not statistically different from the normal subject in those with chest pain but no significant coronary artery stenosis.
anatomic changes such as increased ratio of collagen to elastin, qualitative deficiency of the wall elements, or augmented relative wall thickness due to increases in caliber and wall thickness.\textsuperscript{23} We constructed the nomogram to express the effect of natural aging process on this stiffness index of carotid artery and abdominal aorta by the data from the normal subjects. Stiffness of these two arteries was more elevated than expected from their age in those patients with more extensive coronary artery disease, indicating acceleration of the atherosclerotic process.

Few data on the elastic properties of the human common carotid artery have been published. Arndt and colleagues\textsuperscript{24} measured the pulsatile changes in diameter of the carotid artery with use of the ultrasonic echo technique. Ep calculated from their data of nine subjects was $0.46 \times 10^6$ dynes \cdot cm$^{-2}$ (in 23–34-year-old subjects). Mean Ep value of the common carotid artery of normal control subjects (42–80-year-old subjects) in our study was $1.21 \times 10^6$ dynes \cdot cm$^{-2}$, which is considerably higher than the data obtained by Arndt et al. Although this difference may partly be due to the small number of subjects, the age-related changes on arterial elastic properties from the natural aging process appears to be largely responsible. In the present study, Ep was also increased along with the extent of coronary artery disease. However, standard deviation of Ep in both carotid arteries and abdominal aorta was larger than that of $\beta$ values, especially in patients with three-vessel disease. Coefficient of variation of Ep in abdominal aorta was 0.32, whereas its $\beta$ value was 0.19. The difference between the two values was also the same for carotid artery. The Ep values in patients with two-vessel disease was not significantly augmented. Therefore, the stiffness index we used may provide more reliable information on pathological process of atherosclerosis.

Roberts et al\textsuperscript{7} reported that atherosclerotic plaques were present diffusely in the coronary artery disease of all adult necropsied patients whether with or without symptomatic ischemic heart disease, and similar complicated atherosclerotic plaques were present in the aorta as well. An international cooperative study of distribution of coronary and aortic atherosclerosis in autopsied persons also showed that the different arterial segments develop similar degrees of atherosclerosis, the correlation coefficients of the rankings of location-race groups between segments of the coronary arteries and abdominal aorta being 0.85 or greater.\textsuperscript{2} Though it is impractical to noninvasively assess distensibility of coronary arteries, the measurement of mechanical properties of other major arteries will provide sufficiently accurate information on the sclerotic changes in coronary arteries. Stephanadis et al\textsuperscript{22} measured aortic diameter by angiographic techniques and calculated aortic distensibility as the ratio of changes of aortic diameter to the product of changes of the aortic pressure and those of the diastolic aortic diameter. They demonstrated that patients with coronary artery disease had markedly lower aortic distensibility than normal subjects at

\begin{figure}
\centering
\includegraphics[width=\textwidth]{fig6}
\caption{Bar graphs of arterial stiffness of abdominal aorta and common carotid artery in each group. N, normal control subjects; 0-VD, no significant coronary stenosis; 1-VD, 2-VD, and 3-VD, one-, two-, and three-vessel disease, respectively; bars, SD. *Significant difference from normal control (p<0.05).}
\end{figure}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{fig7}
\caption{Bar graphs of pressure-strain elastic modulus of abdominal aorta and common carotid artery. N, normal control subjects; 0-VD, no significant coronary stenosis; 1-VD, 2-VD, and 3-VD, one-, two-, and three-vessel disease, respectively; bars, SD. *Significant difference from normal control (p<0.05).}
\end{figure}
similar aortic pressures. They suggested reduced vasa vasorum flow from coronary arteries in addition to the common atherosclerotic process as the possible cause of decreased ascending aortic distensibility in coronary artery disease.

Because uncomplicated atherosclerosis seldom accompanies symptoms and brings on death, morphologic studies to prove a clear relation between the measured parameters and actual extent and severity of atherosclerosis is difficult. A nonhuman primate model of atherosclerosis has been used so that changes in arterial elasticity could be related to the actual morphologic changes. Farrar et al\textsuperscript{14} documented increased arterial stiffness in thoracic and abdominal aorta in cynomolgus monkeys fed an atherogenic diet compared with those fed a normal diet in terms of an increased pulse wave velocity. These changes were proportional to morphometric changes of gradual increases in intimal to medial cross-sectional area, the fraction of the intimal elastin lamina being covered with atherosclerotic lesions. It has also been shown by Cox et al\textsuperscript{26} in studies on dietary atherosclerosis in racing greyhounds that arteries from these atherosclerotic animals were stiffer compared with those from control animals during passive conditions as evidenced by the leftward shift of the stress-strain curves. These changes in stiffness were greater in the iliacs than in the carotids and closely correlated with changes in gross morphology of the intima of these segments. All of these data support the view that markedly decreased aortic distensibility may suggest more advanced atherosclerosis. Our observation of the higher prevalence of coronary artery sclerosis in those with more decreased distensibility of abdominal aorta and carotid arteries is consistent with previous observations.

We observed that abdominal aorta is particularly sensitive in differentiating patients with coronary artery disease from the normal subjects. This artery is known to be generally involved much earlier and more intensively in the atherosclerotic process than the other arteries\textsuperscript{27}; this is presumably related to the susceptibility of nutritional deficiency due to lack of penetrating vasa vasorum and its disposition for continuous exposure to unusual physical stress.\textsuperscript{28}

We have used an ultrasonic phase-locked echo-tracking system that allows reliable measurement of pulsatile changes in arterial diameter. Earlier instrumentation permitted arterial wall motion to be measured transcutaneously with an amplitude-tracking method.\textsuperscript{24} But this method was easily subjected to the instability of amplitude and shape of echo signal due to arterial wall motion, artifact from the adjacent tissue, or technical fault to direct the ultrasonic perpendicular to the arterial wall. To eliminate these difficulties, a new phase-locked loop-tracking method was developed.\textsuperscript{18,29} Our method was designed with the aid of control theory to ensure sufficient linearity, dynamic range, and tracking speed, even when the signal-to-noise ratio of the original signal is not high. Thus, this system allows accurate determinations of diameter change by sufficiently stable tracking of the echo signals.

Conclusion

Our new method provides noninvasively sufficiently reliable information on the atherosclerotic damage of large arteries. Our study emphasized the importance of an aortic distensibility as a prognostic indicator of extent of coronary artery disease. The serial noninvasive evaluation of the arterial stiffness allows the early detection of pathologic acceleration of the aging process and may be useful for prevention of coronary artery disease, which constitutes a major atherosclerotic complication.

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