The Prognostic Value of Systolic Time Intervals in Angina Pectoris Patients

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SUMMARY Eighty-five subjects with stable angina pectoris and proven obstructive coronary disease were followed prospectively (mean follow-up 4.2 ± 2.0 years) to assess the value of various predictors of longevity. After patients with congestive heart failure, hypertension, left bundle branch block, valvular heart disease or recent propranolol therapy were excluded, subjects were followed until a major cardiac event (new acute myocardial infarction, cardiac surgery or death) occurred. During follow-up, 22 patients died, 49 survived without events, nine underwent coronary bypass surgery, and five had nonfatal myocardial infarctions. The measurements made at the onset of the study, including cardiothoracic ratio (C/T) on chest x-ray, resting electrocardiographic abnormalities, maximum exercise tolerance testing (METT) data, systolic time interval (STI) measurements (before exercise and 3–4 minutes after METT) and results of cardiac catheterization (55 patients), were analyzed at its conclusion to determine the best predictor of subsequent mortality. Of these measurements, left ventricular ejection fraction, endurance time on METT and C/T were shown to be useful prognostic indicators of subsequent mortality. However, the pre-ejection phase-to-left ventricular ejection time (PEP/LVET) ratio (0.40 ± 0.05 in survivors vs 0.50 ± 0.09 in nonsurvivors) in the resting pre-exercise state was significantly more predictive of mortality than the other measurements. On life-table analysis, the difference in survival between subjects with a resting PEP/LVET < 0.50 and those with a resting PEP/LVET ≥ 0.50 was highly significant. The measurement of the STIs after maximal exercise testing failed to improve upon the prognostic ability of the simple determination of PEP/LVET in the resting, supine state. STIs provided highly specific noninvasive prognostic information in this group of patients with stable angina pectoris.

DEPRESSED LEFT VENTRICULAR function, particularly as reflected in a reduced angiographic ejection fraction (EF) determined at cardiac catheterization, has been shown to affect adversely the prognosis of both medically and surgically treated patients with coronary heart disease. Measurement of systolic time intervals (STIs) is a noninvasive technique that has shown a close correlation with the angiographic assessment of left ventricular performance in most forms of heart disease, although the correlation of the ratio of pre-ejection phase to left ventricular ejection time (PEP/LVET) with EF is not as close in coronary heart disease as it is in certain other forms of heart disease. While several investigators have found the evaluation of ventricular function by STIs to be useful in patients with coronary disease, there has been no prospective study of the relationship between STIs and subsequent mortality in patients with angina pectoris. This study was designed to determine whether STIs, measured before and 3–4 minutes after a maximal exercise treadmill test, have prognostic value in subjects with stable angina pectoris and proven obstructive coronary artery disease.

Methods

Patient Population

Eighty-five patients (80 men and five women), mean age 56 ± 7 years, who were considered by two cardiologists to have stable effort-related angina pectoris, participated in this prospective study of the prognostic value of STI measurements. Stable angina pectoris was diagnosed when recurrent attacks of substernal...
distress of brief duration (less than 10 minutes), brought on by exertion or excitement and relieved by rest or nitroglycerin, were present in a relatively consistent pattern for at least 4 months. The frequency of angina pectoris was determined by having patients record their chest pains in an angina diary during the first month of the study. All patients had either Q-wave electrocardiographic evidence of previous myocardial infarction, as defined by Minnesota criteria (42 patients), or positive coronary arteriograms, as defined by 75% obstruction of at least one major coronary artery (55 patients), or both Q waves and positive arteriograms (28 patients). The 85 subjects had maximal exercise treadmill tests showing ischemic electrocardiographic responses (as defined herein) to exercise, accompanied by either anginal chest pain or an angina equivalent (severe dyspnea developed in three patients with marked ischemic ST depression on the exercise ECG).

All subjects had a baseline clinical evaluation consisting of a complete history, physical examination, chest x-ray, 12-lead ECG, complete blood count, urinalysis and fasting routine blood chemistries to exclude patients with significant disease of other major organ systems. Patients with left bundle branch block on the ECG, coexisting valvular or hypertensive cardiovascular disease, myocardial infarction within 6 months, congestive heart failure or propranolol therapy less than 48 hours before testing were excluded from the study. Twenty-five normal subjects (20 men and five women), mean age 50 years (range 35–63 years), who had no evidence of heart disease by history, physical examination, chest x-ray, ECG or maximal exercise treadmill test, served as normal controls for the study.

Measurement of Systolic Time Intervals

The techniques used in this study to determine STIs before and after a maximal exercise treadmill test were the same as previously reported. All subjects were studied in a fasting state (including abstinence from tobacco and medications) between the hours of 8:00 a.m. and 12 noon. Baseline recordings were made on all 85 patients after they had rested in the supine position for at least 10 minutes. All patients were returned to the supine position for STI recordings 3–4 minutes after maximal exercise. The ECG, the phonocardiogram and the carotid arterial pulse were recorded simultaneously at a paper speed of 200 mm/sec, with 20-msec time lines on a DR-8 Electronics for Medicine research recorder. The ECG consisted of a single bipolar chest lead (CB), described below. When CB failed to show a well-delineated onset of QRS, the standard limb lead that best defined the onset of electrical depolarization was used. The phonocardiogram was obtained with a contact microphone (Electronics for Medicine) placed at the point on the anterior chest wall showing the best definition of the second heart sound. The carotid pulse recording was made by placing a funnel air-coupled to a pressure transducer (Statham P23Db) over the carotid artery.

Total electromechanical systole (QS₂) was measured from the onset of the QRS complex to the first high-frequency vibrations of the aortic closure sound. Left ventricular ejection time (LVET) was measured from the beginning of the rapid upstroke of the carotid pulse tracing to the incisural notch. The pre-ejection phase (PEP) was determined by subtracting the LVET from QS₂. The STI indices (QS₂I, LVETI and PEPI) were derived by averaging the measurements of 10 consecutive beats determined to the nearest 5 msec, and applying the appropriate regression equations of Weissler. Since STIs were determined when the patient entered the study, neither the technician making the measurements nor the cardiologist rechecking the measurements had knowledge of the patient’s subsequent clinical course.

Maximal Exercise Treadmill Testing

After resting STIs were recorded, all subjects performed maximal exercise treadmill tests, as described by McDonough and Bruce. Subjects walked on the treadmill to the point of chest pain or other limiting symptoms such as dyspnea or fatigue. Chest lead CB, a single, bipolar lead with the positive electrode at the V₅ position and the negative electrode over the right scapula, was used for continuous electrocardiographic monitoring. ECGs and cuff blood pressures were recorded at baseline, during each minute of exercise and during at least the first 5 minutes of recovery. Baseline 12-lead ECGs were blindly interpreted according to the Minnesota Code for resting ECGs. An ECG was considered to show an ischemic response to exercise if the ST segment developed at least 1 mm depression (horizontal or downward sloping for at least 0.08 second) below or elevation above the PR segment.

Cardiac Catheterization

Fifty-five subjects underwent clinically indicated cardiac catheterization for evaluation of angina pectoris. Left ventricular end-diastolic pressure was obtained with a Statham P23Db transducer and cardiac index was measured by the indocyanine green dye technique. Left ventricular volumes and EFs were determined according to the method of Greene et al., from single-plane, 35-mm cineangiograms filmed at 60 frames/sec in the right anterior oblique projection. Abnormalities of left ventricular wall motion on the cineangiograms were evaluated according to American Heart Association guidelines by grading the anterior, apical and inferior segments of the left ventricle as normal, hypokinetic, akinetic, or dyskinetic.

Selective coronary arteriographic studies, performed by means of the percutaneous femoral approach and the Judkin technique, were filmed in multiple projections of each coronary artery to assure adequate visualization of the entire coronary circulation of each patient. All arteriograms were "blindly" interpreted when the patient entered the study by a cardiologist ex-
experienced in interpreting coronary arteriograms who had no knowledge of the results of the STI measurements. The degree of coronary obstruction was graded by careful visual inspection from 0–100% for the left main coronary artery, the left anterior descending coronary artery, the major diagonal branches, the circumflex coronary artery, the major circumflex marginal branches, the right coronary artery and the posterior descending coronary artery. A vessel was classified as significantly obstructed when there was at least 75% narrowing of the lumen and the obstructing lesion was present in more than one projection.

Patient Follow-Up and Data Analysis

After initial evaluation and STI determination, these patients were followed by the principal investigator in the cardiology clinic (78 patients) or by physicians at other facilities (seven patients) for periods ranging from 3 months to 6 years (mean 4.2 ± 2.0 years). Clinical follow-up periods were terminated on the date of new nonfatal myocardial infarctions (five patients) or coronary bypass surgery (nine patients), since such events may alter left ventricular function. Information about the circumstances of a patient’s death was obtained from hospital records, from other physicians involved in the patient’s care and from the patient’s family. When a patient moved from the area or was under the care of a physician at another facility, data were obtained by written communication and by telephone conversation with the patient, his family and his physician. The diagnosis of new myocardial infarction required the presence of unequivocal electrocardiographic changes of myocardial infarction not present on previous ECGs or elevation of serum enzymes indicating myocardial necrosis or both, associated with a prolonged chest pain consistent with infarction.

Data analysis was performed on a Digital Equipment Corporation PDP 11–34 computer using standard, well-tested FORTRAN statistical subroutines converted to double-precision arithmetic. Point biserial correlation coefficients were calculated to compare variable means of survivors vs nonsurvivors. Chi-squared testing was performed on ECG reading results in both Z × 2 form (using the Yates correction) and in Z × k form. Simple and multiple linear regression was calculated to determine relationship between pairs and groups of variables. Finally, life-table analysis of groups separated by their results on STI testing, exercise tolerance testing, cardiothoracic ratio and cardiac catheterization results were performed.

Results

Table 1 shows the survival data on these 85 patients with angina pectoris. Twenty-two patients (21 men and one woman) died during the follow-up period. It is highly likely that coronary heart disease contributed in a major way to the death of these patients. The cause of death in 12 patients was acute myocardial infarction, confirmed by clinical data during hospitalization (nine patients) and/or autopsy findings (five patients). Eight deaths were classified as sudden because death occurred before the patient could be hospitalized. The autopsy on one patient who had a prolonged hospitalization for bronchogenic carcinoma showed the cause of death to be severe congestive heart failure without cardiac metastases. One patient who had infrequent angina pectoris and no previous evidence of ventricular arrhythmia was killed when he lost control of his vehicle and collided with an embankment. There were 14 surviving patients whose follow-up was terminated at the time of acute myocardial infarction (five patients) or coronary bypass surgery (nine patients). The remaining 49 patients (48 men and one woman) survived without any major events.

Systolic Time Intervals Data

The results of the STI determinations, before and 3–4 minutes after maximal exercise treadmill testing, in the 85 subjects with angina pectoris and 25 normal subjects are shown in tables 2 and 3. There were statistically significant differences in the STI values between the normal subjects and the angina pectoris patients, as well as between the patients who survived and those who died. In angina pectoris patients vs normals and in nonsurvivors vs survivors, the values for PEP/LVET and PEPI were significantly greater, both before and after exercise. These differences in mean STI measurements are consistent with left ventricular impairment in the angina pectoris subjects as a whole and in the nonsurvivors in particular. While a substantial number (24 of 63) of the survivors also had diminished left ventricular function, as indicated by mean STI measurements that differed significantly ($p < 0.001$) from the values in the 25 normal subjects, the nonsurvivors had a greater degree of left ventricular impairment. Although resting PEPI was significantly greater and LVETI was shorter in patients who died, the PEP/LVET was the best prognostic parameter in these 85 subjects. The change in STIs from the resting to the postexercise state showed significant differences between normals and angina pectoris patients. Angina pectoris patients had significantly prolonged LVETI ($p < 0.005$), while normal subjects had slightly shortened LVETI after exercise. The determination of LVETI before and after ex-

| Table 1. Survival Data on 85 Patients with Angina Pectoris |
|---------------------------------|-----------------|
| Status                          | Mean follow-up  |
| Dead (22 patients)              | 2.0 ± 1.1       |
| Acute myocardial infarctions (12)|                |
| Sudden deaths (outside hospital) (8) |                |
| Congestive heart failure (1)    |                |
| Automobile accident (1)         |                |
| Alive (63 patients)             | 4.7 ± 1.5       |
| Survived without major events (49) |                |
| Nonfatal myocardial infarctions (5) |                |
| Coronary bypass surgery (9)     |                |

- TABLE 1. Survival Data on 85 Patients with Angina Pectoris
- CIRCULATION
- VOL 60, NO 2, AUGUST 1979
LVET indices, change testing left ventricular (msec) QS2I clinical significant (p

2.

PEP/LVET

Before 0.36 ± 0.03 0.43 ± 0.08 <0.001

After 0.31 ± 0.05 0.35 ± 0.08 <0.001

PEPI (msec)

Before 135 ± 6 148 ± 16 <0.001

After 112 ± 11 129 ± 19 <0.001

LVETI (msec)

Before 416 ± 9 394 ± 16 <0.001

After 411 ± 13 413 ± 21 NS

Values for normals and patients are mean ± s.d.

P value refers to difference between normals and patients. Abbreviations: PEP/LVET = ratio of pre-ejection phase to left ventricular ejection time; PEPI = pre-ejection phase index; LVETI = left ventricular ejection time index; QS2I = total electromechanical systole index; NS = not statistically significant (p > 0.05).

Exercise testing has been reported as a clinically useful diagnostic technique for obstructive coronary disease in patients with chest pain. Of the various STI measurements (including STI indices, change in STI indices from the resting to the postexercise state and heart rates at rest and after exercise) subjected to statistical analysis, PEP/LVET measured before exercise correlated best with subsequent mortality. A resting PEP/LVET ≥ 0.50 (the mean for nonsurvivors) separated out a group of patients with increased mortality risk. Fourteen of the 22 patients who died during follow-up had PEP/LVET ≥ 0.50, while only two of the 63 survivors had such high values for the pre-exercise PEP/LVET. Therefore, an increase in PEP/LVET to 0.50 or greater, a value considered indicative of moderately severe depression of left ventricular function in coronary disease, proved to be an accurate predictive index of poor prognosis in the 85 patients with angina pectoris. The measurement of the STIs 3–4 minutes after maximal exercise testing provided no additional prognostic information.

The results of life-table analysis relating survival to resting PEP/LVET ≥ 0.50 and resting PEP/LVET of 0.50 is shown in figure 1. At all points on the life-table, the difference in survival between those with PEP/LVET ≥ 0.50 compared with PEP/LVET < 0.50 is highly significant. The analysis includes the 14 living patients (mean PEP/LVET 0.41 ± 0.07), whose follow-up periods were terminated on the date of new, nonfatal myocardial infarction or coronary bypass surgery. Exclusion of these 14 patients did not significantly influence the results of the life-table analysis. The median survival time of 10 months for subjects with PEP/LVET ≥ 0.50 indicates that persons with this abnormality usually died in the early follow-up period (i.e., such subjects had a 50% chance of dying in the first 10 months of follow-up). However, patients with a PEP/LVET < 0.50 had a median survival of longer than 60 months.

The approximately parallel relationship of the two survival curves after 30 months of follow-up shows that patients with early mortality (before 30 months) had the greatest abnormality in PEP/LVET. Patients who died during the first 18 months of the study had significantly (p < 0.05) greater abnormality in PEP/LVET (0.56 ± 0.08) than patients who died after 30 months of follow-up (PEP/LVET 0.46 ± 0.08). Thus, the data on these 85 patients with angina pectoris who were followed a mean of 4.2 years show that such patients with a resting PEP/LVET ≥ 0.50 are at significantly increased risk of death, and that patients with the greatest abnormality of resting PEP/LVET are at the greatest risk of early death.

Other Test Data

The results of analysis of various parameters as predictors of mortality in these 85 patients with angina pectoris are shown in table 4. Those parameters showing correlation with subsequent mortality included: angiographic left ventricular EF, endurance time on the treadmill, cardiothoracic ratio > 0.50 determined from the standard chest x-ray, and a history of smoking cigarettes (defined as 20 or more cigarettes per day) at the time of entry into the study. Life-table analysis of these parameters — shown in
previous studies to yield prognostic information in coronary patients — did not provide an estimated probability of survival as reliable as that provided by the resting PEP/LVET data.\textsuperscript{1, 17, 18} In the following parameters, there were no statistically significant differences between survivors, nonsurvivors and patients who had major nonfatal events: age at entry into the study, frequency of angina pectoris, resting blood pressure, fasting blood sugar (or incidence of diabetes mellitus) or serum cholesterol level. Abnormalities on the resting 12-lead ECGs obtained on the 85 patients at entry into the study were not significantly different between survivors and nonsurvivors when the following findings were compared: ventricular arrhythmia, high-amplitude R wave, abnormal Q wave, ST depression, ST elevation and negative T waves.\textsuperscript{19}

Cardiac catheterization data on 55 of the 85 patients showed that of the various parameters studied, only an abnormally low angiographic left ventricular EF correlated significantly with an increased risk of mortality. The left ventricular EF, a well-established angiographic measure of ventricular function, was significantly \((p < 0.005)\) lower in patients who died (10 studied) (EF 0.42 ± 0.16) than in those who survived (35 studied) (EF 0.57 ± 0.11), thus confirming that poor left ventricular function was a major determinant of the increased risk of mortality in these patients with coronary disease. There was a correlation \(r = -0.57\) between EF and resting PEP/LVET, but not as good as has been reported in certain other forms of heart disease.

While there are fewer patients in the present study than in that of Lewis et al. (who reported a somewhat better correlation of EF and PEP/LVET), the current investigation provided a relatively wide distribution of data points for analysis.\textsuperscript{8} The frequency of abnormalities of ventricular wall motion (hypokinesis, akinesia or dyskinesia) detected on cineangiography was higher in patients who died (10 of 11; 90\%) than in patients who survived (21 of 39; 54\%), but this difference was not statistically significant.

These data are subject to the limitations of single-plane, right anterior oblique cineangiography for evaluation of the presence and extent of left ventricular wall motion abnormalities. There were not enough patients who had the additional left anterior oblique view to include data on septal and posterolateral wall motion abnormalities. Selective coronary arteriograms showed no statistically significant difference in the extent of coronary disease (i.e., number of vessels obstructed) between survivors and nonsurvivors, although there were more subjects with three or more coronary arteries obstructed among those who died. Of 42 patients who survived, 15 (36\%) had significant obstruction of three or more coronary arteries, while nine of 13 (69\%) patients who died had extensive three-vessel coronary disease at entry into the study. This tendency toward higher mortality among patients with more extensive coronary disease might possibly have achieved statistical significance, as has been reported in studies involving larger numbers of patients, if more of the subjects who died had coronary arteriograms available for inclusion in the data analysis.\textsuperscript{20, 21} There were no significant differences in the left ventricular end-diastolic pressures or cardiac indices between survivors and nonsurvivors.

The data from the maximal exercise treadmill tests in these 85 patients were analyzed to determine


**Table 4. Summary of Test Data in 85 Angina Pectoris Patients**

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Survivors (n = 63)</th>
<th>Nonsurvivors (n = 22)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEP/LVET (basal)</td>
<td>0.40 ± 0.05</td>
<td>0.50 ± 0.09</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Angiographic EF</td>
<td>0.57 ± 0.11</td>
<td>0.42 ± 0.16</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>METT Time (min)</td>
<td>5.3 ± 1.0</td>
<td>4.2 ± 1.2</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>C/T &gt; 0.50</td>
<td>17/63 (27%)</td>
<td>12/22 (54%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>12/63 (19%)</td>
<td>10/22 (45%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Age at entry</td>
<td>55.6 ± 6.7</td>
<td>55.9 ± 8.1</td>
<td>NS</td>
</tr>
<tr>
<td>Angina frequency</td>
<td>6.1 ± 9.5</td>
<td>10.2 ± 12.7</td>
<td>NS</td>
</tr>
<tr>
<td>(pains/week)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>131 ± 13.6</td>
<td>128 ± 18.7</td>
<td>NS</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>83 ± 7.7</td>
<td>82 ± 10.2</td>
<td>NS</td>
</tr>
<tr>
<td>Fasting blood sugar (mg%)</td>
<td>105 ± 14.1</td>
<td>110 ± 17.0</td>
<td>NS</td>
</tr>
<tr>
<td>Serum cholesterol (mg%)</td>
<td>254 ± 48.7</td>
<td>244 ± 33.4</td>
<td>NS</td>
</tr>
<tr>
<td>ECG abnormalities</td>
<td>81/99 (81%)</td>
<td>44/48 (92%)</td>
<td>NS</td>
</tr>
<tr>
<td>Wall motion abnormalities</td>
<td>21/39 (54%)</td>
<td>10/11 (90%)</td>
<td>NS</td>
</tr>
<tr>
<td>Three-vessel coronary disease</td>
<td>15/42 (36%)</td>
<td>9/13 (69%)</td>
<td>NS</td>
</tr>
<tr>
<td>LVEDP (mm Hg)</td>
<td>11.4 ± 5.1</td>
<td>14.6 ± 3.4</td>
<td>NS</td>
</tr>
<tr>
<td>Cardiac index (1/min/m²)</td>
<td>2.6 ± 0.4</td>
<td>2.4 ± 0.6</td>
<td>NS</td>
</tr>
<tr>
<td>ST shift on METT (mm)</td>
<td>-1.9 ± 1.2</td>
<td>-1.5 ± 1.9</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values for survivors and nonsurvivors are mean ± sd.
Abbreviations: PEP = pre-ejection phase; LVET = left ventricular ejection time; EF = ejection fraction; METT = maximal exercise treadmill test; C/T = cardiothoracic ratio; NS = not significant (p > 0.05); LVEDP = left ventricular end-diastolic pressure; BP = blood pressure.

differences between survivors and nonsurvivors and to identify parameters showing prognostic information. Bruce reported the following exercise testing data to have prognostic implications: duration of exercise, maximal systolic blood pressure during exercise, exertional arrhythmia and abnormalities in the resting ECG. Analysis of these exercise parameters in the present study showed only duration of exercise to be significantly different (p < 0.01) when survivors were compared with nonsurvivors. Subjects who survived had greater endurance on the treadmill than subjects who died (5.3 ± 1.0 minutes vs 4.2 ± 1.2 minutes). An endurance time on the treadmill of less than 3 minutes indicated a poor prognosis, since five of seven patients with this abnormality died during follow-up.

Failure to maintain a maximum systolic blood pressure of at least 130 mm Hg during exercise testing, which Bruce reported to carry a poor prognosis, was present in only one of the 85 patients, who died suddenly after 11 months follow-up. While there were no significant mean differences between survivors and nonsurvivors in the degree of ST shift induced by exercise testing, three of eight subjects with very marked ischemic ST depression (4 mm or more) induced by exercise died during the study. Comparison of the prognostic abilities of these various exercise parameters with the STI measurements by a point biserial correlation coefficient calculation showed the PEP/LVET to be by far the best indicator of prognosis.

There was a significantly (p < 0.05) greater incidence of cardiac enlargement, as defined by a cardiothoracic ratio > 0.50 on the standard chest x-ray, in patients who died (12 of 22; 54%) compared with those who survived (17 of 63; 27%). While cardiac enlargement had prognostic implications, life-table analysis comparing subjects with a cardiothoracic ratio > 0.50 with those with a cardiothoracic ratio ≤ 0.50 showed that this measurement from the standard chest x-ray did not discriminate between survivors and nonsurvivors as well as the STI data (i.e., PEP/LVET). During the first 6 months of the study, life-table analysis showed no significant difference in survival between those with cardiac enlargement thus defined and those with normal heart size, while similar analysis using PEP/LVET ≥ 0.50 compared with PEP/LVET < 0.50 showed a highly significant difference between survivors and nonsurvivors in the same time period. There was no statistically significant difference in the mean values for the cardiothoracic ratio of the 63 patients who survived and the 22 patients who died (0.48 ± 0.05 vs 0.50 ± 0.06, respectively).

**Discussion**

Undoubtedly, left ventricular function is a major determinant of short-term prognosis in patients with coronary heart disease. Patients with angina pectoris who have evidence of depressed left ventricular function at cardiac catheterization are at higher risk of mortality, whether treated medically or surgically, than patients with normal left ventricular function. Among the various hemodynamic and angiographic parameters studied in 144 medically treated patients with coronary disease, Nelson et al. found left ventricular EF to be the most powerful predictor of short-term survival. In that study, subjects with an abnormally low EF (< 0.50) had a significantly higher mortality (33% vs 12%) during 14 months of follow-up. Hammermeister et al. reported that of the various testing parameters studied in 160 patients undergoing direct myocardial revascularization for coronary disease, only parameters relating to left ventricular performance were predictive of operative mortality. In particular, an EF of 33% or less was found to increase the risk of surgical mortality in their patients.

A number of noninvasive parameters that largely reflect ventricular performance have been shown to have prognostic value in patients with coronary heart disease. A recently published study of 320 patients with various forms of heart disease indicates that cardiothoracic ratio and plain film heart volume obtained from the chest x-ray are useful noninvasive mea-
measurements for evaluating left ventricular function and for determining prognosis. Although only 11% of the patients in that study had coronary heart disease, the actuarial survival curves showed the measurements made on the standard chest x-ray to be highly predictive of long-term (mean follow-up 4.1 years) survival. Bruce emphasized the value of exercise testing for evaluation of ventricular function and noted that mortality rate due to coronary disease can be related to duration of exercise, exertional arrhythmias, maximal systolic blood pressure with exercise, cardiomegaly and the number of abnormalities on the resting electrocardiogram. While an ischemic ST response to exercise has prognostic implications, it appears that parameters of the exercise test relating more directly to ventricular function (e.g., a duration of exercise of less than 3 minutes or a failure to attain a maximum systolic pressure of at least 130 mm Hg) contain stronger prognostic information than the ST segments of the exercise ECG.

Although the STI technique for evaluating ventricular performance has been reported to have prognostic value in patients with acute myocardial infarction, and several investigators have shown the technique to be a valid and sensitive means of detecting left ventricular dysfunction in chronic coronary disease patients, there has been no prospective study to determine the predictive ability of this noninvasive method in patients with stable angina pectoris. There are conflicting reports about the usefulness of STIs in acute myocardial infarction, but several investigators have found that patients with the greatest abnormality of PEP/LVET have the most severe impairment of left ventricular function and the highest mortality rate. Stack et al., in a study of 37 patients with prior transmural myocardial infarction, found STIs to be superior to clinical bedside methods (i.e., history, physical examination, phonocardiogram, ECG and chest x-ray) in evaluating performance of the left ventricle. Lewis et al., in a study of 127 patients with angiographically documented chronic coronary artery disease, found a correlation \( r = -0.76 \) between angiographic left ventricular EF and the PEP/LVET of STIs. In 95% of their cases, a PEP/LVET > 0.50 was associated with an EF < 40%. While depressed left ventricular function of that degree would be expected to be associated with increased mortality rate, these authors did not report prospective follow-up information for their patients.

Although angiographic EF is considered by some investigators to be the most useful predictor of short-term survival in coronary patients, the regional contraction abnormalities in this form of heart disease may distort the ellipsoid configuration of the ventricle and thus reduce the accuracy of this method to evaluate left ventricular performance. Similarly, the single-plane echocardiogram is limited in estimating left ventricular function in coronary disease because segmental myocardial involvement occurs in this disorder. Although STIs are not highly correlated with angiographic EF, they are not dependent upon the geometry of the left ventricle and offer an alternative means of evaluating left ventricular performance that stands on its own merit. The present study of 85 patients with stable angina pectoris followed prospectively for more than 4 years provides evidence not only for the validity of STIs as a means of detecting left ventricular dysfunction in subjects with coronary disease, but also shows the method to have very significant prognostic value.

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References

The prognostic value of systolic time intervals in angina pectoris patients.
R E Gillilan, W P Parnes, M A Khan, R J Bouchard and J R Warbasse

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