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Interactive Effects of ST-T Wave Abnormalities on Survival of Patients With Coronary Artery Disease

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Previous studies have documented a reduced survival time in patients with an electrocardiographic (ECG) ST-T wave abnormality. This study was designed to determine the clinical, hemodynamic and angiographic correlates of this observation. Data from 9,731 patients undergoing cardiac catheterization from 1976 through 1986 were analyzed; 5,531 had severe (>70%) obstruction of at least one major coronary artery, 1,706 had mild (10 to 69%) obstruction and 2,494 had no obstruction. Of the patients with severe obstruction, 2,536 were treated medically and 2,995 were treated by surgical revascularization.

Patients with an ST-T abnormality had more clinical risk factors (including older age and greater prevalence of diabetes mellitus, hypertension and prior myocardial infarction) and greater left ventricular dysfunction (including higher end-diastolic pressure and ventricular volume, reduced ejection fraction and greater prevalence of contraction abnormality) than did those without this ECG pattern. Survival time was significantly ($p < 0.01$) reduced in subsets of patients with an ST-T abnormality and with severe or mild coronary artery disease; in those without coronary disease, ST-T changes did not correlate with reduced survival.

Stepwise regression analysis was applied to each group to determine the independent predictors of 5-year survival. In patients with severe disease or no disease, an ST-T abnormality was not chosen as an independent predictor of 5-year survival; in the group with mild disease, ST-T changes were an independent predictor of reduced survival. Thus, the independent impact of an ST-T abnormality on survival is dependent on the severity of underlying coronary artery disease.

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Population studies (1–5) have demonstrated that an ST-T wave abnormality on the rest electrocardiogram (ECG) is associated with a reduced survival rate. For example, Cullen et al. (3) in the Busselton study showed that, after 13 years of follow-up, the 2,100 patients 40 to 79 years old whose initial ECG showed ST segment depression or inverted, flattened or biphasic T waves had a higher mortality rate than that of the patients with a normal initial ECG. Similarly, Kannel et al. (5) in the Framingham study found that the rates for age-adjusted coronary heart disease morbidity and mortality were nearly doubled in patients with compared with those without ST-T abnormalities.

These studies typically relied on clinical assessments to predict the presence of coronary artery disease. Angiographic documentation of the extent of obstruction and the status of cardiac function—both known to affect survival of patients with coronary artery disease (6,7)—have been lacking. Many patients with symptoms suggesting coronary artery disease do not have vascular obstructions and in those who do, the extent of disease may be highly variable even when the clinical presentation is similar. In this study we examined the effect on survival of the interactions of ST-T wave abnormalities with these anatomic and functional variables.

Methods

Selection of patients. Cases were selected from 18,958 patients undergoing cardiac catheterization at the Baptist Memorial Hospital in Memphis, Tennessee between 1976 and 1986. Clinical, ECG, angiographic and hemodynamic data were prospectively entered into a computerized data base. In addition, follow-up data were acquired yearly on all patients by mail questionnaire addressed to the patient or, if the patient did not respond, to the referring physician.

Cardiac catheterization. Coronary angiograms were performed by routine methods and were interpreted by hospital staff cardiologists. Ventricular volumes and left ventricular ejection fractions were computed with single-plane methods. Abnormal left ventricular contraction was diagnosed if akinesia or dyskinesia was found in any of eight segments of the left ventricular contour. No major changes in technique were introduced during the study period and no specific efforts to standardize procedures were attempted.

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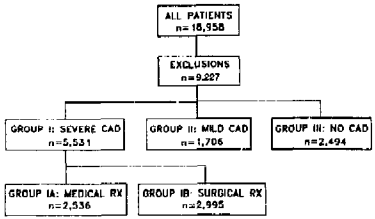

Figure 1. Outline of the study group and subgroups. CAD = coronary artery disease; medical Rx = medical therapy; surgical Rx = surgical therapy.

Electrocardiography. Electrocardiograms were interpreted by computer (Marquette Electronics) and the results reviewed by staff cardiologists. An ST-T wave abnormality was considered to be present if ST segment depression (≥100 μV 60 ms after the J point with use of a TP segment baseline) with or without abnormal T wave inversion was present in the ECG recorded immediately before catheterization. Final interpretations after review were entered into the data base.

Risk factors. Risk factor data were abstracted from the clinical record. Factors studied included history of diabetes mellitus (defined by history of or therapy of hyperglycemia), hypercholesterolemia (defined by total plasma cholesterol ≥240 mg/100 ml), systemic hypertension (defined by history of treatment or arterial pressure ≥160/90 mm Hg) and current cigarette use, as well as age, gender and race.

Exclusion criteria. Patients were excluded if 1) they had a diagnosis of congenital, significant valvular or primary myocardial disease; 2) they had ECG evidence of complete or incomplete bundle branch block, left posterior fascicular block, Wolff-Parkinson-White syndrome, Q wave myocardial infarction or paced rhythm; 3) they had died during the hospital stay; 4) they had undergone cardiac surgery before the first recorded cardiac catheterization; or 5) they had <5 years of complete follow-up.

Patient groups. On the basis of these criteria, 9,731 patients were selected. They were classified into three groups on the basis of severity of coronary artery disease (Fig. 1). *Group I* included 5,531 patients with at least one >70% obstruction in a major epicardial vessel or an obstruction >50% in the left main coronary artery. This group was further classified into two subgroups based on treatment prescribed by the patients' attending physician. Group IA consisted of 2,536 patients receiving medical treatment and Group IB included 2,995 patients who underwent surgical revascularization with either saphenous vein or internal mammary artery implantation.

Group II consisted of 1,706 patients with mild disease, defined as at least one obstruction of a major epicardial vessel >10% but no obstruction >70% and <50% obstruction of the left main coronary artery. *Group III* included 2,494 subjects with no obstruction in any vessel >10%.

Statistical analysis. Data analysis relied on standard univariate and multivariate techniques. Univariate analysis included chi-square tests for categoric variables and *t* tests for continuous ones. Multivariate analyses incorporated a stepwise selection method for discriminant function analysis (SPSS^X) with p in = p out = 0.01. In addition, life-table survival analysis was applied to patient subgroups; the Lee-Desu statistic was used for multiple comparisons of survival between subgroups.

Results

A total of 4,316 of the 9,731 patients had an ST-T wave abnormality. This included 2,804 patients (50.7% of Group I) with severe, 702 (41.1% of Group II) with mild and 810 (32.5% of Group III) with no coronary disease. Of those with severe disease, ST-T changes were found in 1,252 (49.4% of Group IA) treated medically and in 1,552 (51.8% of Group IB) treated surgically.

Demographic and clinical data (Tables 1 to 4). The 4,316 patients with an ST-T abnormality and 5,415 patients without the abnormality differed with respect to several variables (Table 1). Patients with an ST-T abnormality were older and a greater proportion were female, non-white, hypertensive, diabetic, cigarette smokers and had a history of myocardial infarction. Hypercholesterolemia was the only assessed feature that was not significantly more common in the subgroup with an ST-T abnormality.

The prevalence of these characteristics was also evaluated in each of the patient subgroups (Tables 2 to 4). Only minor differences were apparent. In patients with mild coronary artery disease (Group II), cigarette smoking was not more common in patients with than in those without an ST-T abnormality and the age of patients with and without an ST-T change was similar in the group without coronary disease (Group III).

Angiographic and hemodynamic data. When all patients were considered together (Table 1), the presence of an ST-T wave abnormality predicted a significantly lower left ventricular ejection fraction (tabulated as both the group mean and the percent of patients with values <50%) and higher left ventricular end-systolic volume index, end-diastolic volume index, left ventricular end-diastolic pressure and prevalence of abnormal left ventricular contraction than if the ST-T wave were normal.

When the groups are classified on the basis of severity of coronary obstruction (Tables 2 to 4), the presence of an ST-T wave abnormality also corresponded to more left ventricular functional disorders. In Group I patients with severe stenosis (Table 2), those with an ST-T abnormality had a significantly lower ejection fraction, higher ventricular volumes and end-diastolic pressures and a higher prevalence of contraction abnormalities. However, there was no signifi-

Table 1. Hemodynamic and Angiographic Features of All Patients Included in the Study

Characteristics	All Patients		
	Total	−STT	+STT
Clinical			
Number of patients	9,721	5,415	4,316
Age (yr, mean ± SEM)	56.0 ± 0.1	55.1 ± 0.2	57.1 ± 0.2*
Gender (% male)	63.6	66.4	60.1*
Race (% white)	88.5	90.5	86.1*
Hypertension (%)	46.0	53.6	48.0*
Diabetes (%)	10.9	8.9	13.4*
Hypercholesterolemia (%)	33.3	32.4	34.1
Smokers (%)	57.0	52.9	62.2*
History of MI (%)	21.6	16.4	28.2*
Angiographic and hemodynamic			
LV ejection fraction			
Mean ± SEM	65.9 ± 0.1	66.9 ± 0.2	64.8 ± 0.2*
<50% (%)	9.8	7.6	12.4*
End-systolic volume index ≥34 ml/m² (%)	26.2	22.8	30.3*
End-diastolic volume index >90 ml/m² (%)	26.6	24.2	29.6*
End-diastolic pressure ≥15 mm Hg (%)	28.5	25.8	31.7*
Abnormal contraction (%)	35.2	28.9	43.0*

*$p < 0.01$, patients with (+STT) versus patients without (−STT) an ST-T wave abnormality. LV = left ventricular; MI = myocardial infarction.

cant difference in the number of diseased vessels between subsets with and without an ST-T abnormality (2.47 ± 0.02 vs. 2.33 ± 0.02 vessels, mean ± SEM).

Group I was divided into medically (Group IA) and surgically (Group IB) treated subgroups. Patients in Group IA had less severe coronary artery disease (2.17 ± 0.01 vessels obstructed) than did those in Group IB (2.60 ± 0.01 vessels obstructed, $p < 0.05$). In each subgroup, those with

Table 2. Clinical, Hemodynamic and Angiographic Data of Patients With Severe Coronary Obstruction (Group I)

Characteristics	Total			Group IA		Group IB	
	Total	−STT	+STT	−STT	+STT	−STT	+STT
Clinical							
Number	5,531	2,727	2,804	1,284	1,252	1,443	1,552
Age (yr, mean ± SEM)	58.2 ± 0.1	57.5 ± 0.2	58.8 ± 0.2*	57.2 ± 0.3	58.5 ± 0.3*	57.6 ± 0.3	59.1 ± 0.3*
Gender (% male)	75.4	79.3	71.5*	76.9	67.1*	81.5	75.1*
Race (% white)	90.2	91.8	88.8*	90.7	86.4*	92.8	90.3*
Hypertension (%)	42.6	36.5	48.6*	37.2	49.5*	35.8	47.8*
Diabetes (%)	13.5	11.7	15.1*	12.1	15.5*	11.4	14.8*
Hypercholesterolemia (%)	36.5	36.5	36.5	34.1	35.1	38.9	37.7
Smokers (%)	64.5	59.5	69.3*	62.3	68.7*	57.0	69.7*
History of MI (%)	33.3	28.1	38.4*	30.8	43.8*	25.6	34.0*
Angiographic and hemodynamic							
coronary artery disease							
One-vessel	2,081	1,086	995	718	653*	368	342
Two-vessel	1,692	838	854	373	343*	465	511
Three-vessel	1,233	557	676	147	197*	410	479
Left main	525	246	279	46	59*	200	220
LV ejection fraction							
Mean ± SEM	63.2 ± 0.2	64.3 ± 0.3	62.2 ± 0.3*	63.9 ± 0.4	62.3 ± 0.4*	64.7 ± 0.4	62.1 ± 0.4*
<50% (%)	15.5	12.8	18.2*	13.8	18.5*	12.0	17.8*
End-systolic volume index ≥34 ml/m² (%)	34.3	30.9	37.9*	31.9	37.3*	30.2	38.4*
End-diastolic volume index ≥90 ml/m² (%)	31.0	28.2	33.8*	29.0	33.6*	27.6	34.0*
End-diastolic pressure ≥15 mm Hg (%)	35.9	32.9	38.9*	32.1	37.2*	33.6	40.2*
Abnormal contraction (%)	54.5	48.4	60.4*	50.7	58.4*	46.1	61.9*

*$p < 0.01$. +STT versus − STT. Group I = patients with severe disease; Group IA = patients with severe disease treated medically; Group IB = patients with severe disease treated surgically. Abbreviations as in Table 1.

Table 3. Clinical, Hemodynamic and Angiographic Data of Patients With Mild Coronary Artery Stenosis (Group II)

Characteristics	Total	−STT	+STT
Clinical			
Number	1,706	1,104	702
Age (yr, mean ± SEM)	56.0 ± 0.3	55.3 ± 0.3	57.0 ± 0.4*
Gender (% male)	53.0	59.3	44.2*
Race (% white)	88.3	89.8	86.2*
Hypertension (%)	45.3	40.5	52.1*
Diabetes (%)	9.3	7.6	13.4*
Hypercholesterolemia (%)	32.9	33.0	32.8
Smokers (%)	57.5	58.7	55.8
History of MI	8.1	7.0	9.8*
Angiographic and hemodynamic			
LV ejection fraction			
Mean ± SEM	69.9 ± 0.2	69.7 ± 0.3	70.1 ± 0.4*
<50% (%)	1.6	1.8	1.3
End-systolic volume index ≥34 ml/m²	12.8	12.5	13.4
End-diastolic volume index ≥90 ml/m²	19.4	19.1	20.0
End-diastolic pressure ≥15 mm Hg	18.7	17.8	19.9
Abnormal contraction (%)	12.3	12.8	11.4

*$p < 0.01$, +STT versus −STT. Abbreviations as in Table 1.

an ST-T abnormality had a significantly lower ejection fraction, higher ventricular volumes and end-diastolic pressures and a higher prevalence of contraction abnormalities. Patients in Group IA with an ST-T abnormality also had more extensive coronary disease (2.23 ± 0.02 vessels obstructed) than did those without this abnormality (2.11 ± 0.02 vessels obstructed); in Group IB, however, the extent of disease was similar in those with (2.66 ± 0.02 vessels obstructed) and without (2.53 ± 0.02 vessels obstructed) an ST-T change.

In patients with mild disease (Group II), mean left ventricular ejection fraction was the only factor that differed significantly between those with and without an ST-T abnormality (Table 3). In patients in Group III with no coronary artery disease, the prevalence of low left ventricular ejection fraction and of abnormal contraction was higher in those with than in those without an ST-T abnormality (Table 4).

Effects of ST-T abnormality on survival. Survival of the 4,316 patients with an ST-T abnormality was compared with that of the 5,415 patients without an ST-T abnormality. A significant ($p < 0.01$) decrease in 5-year survival was found in those with the ECG abnormality (Fig. 2). After 5 years of

Table 4. Clinical, Hemodynamic and Angiographic Data of Patients With No Coronary Artery Stenosis (Group III)

Characteristics	Total	−STT	+STT
Clinical			
Number	2,494	1,684	810
Age (yr, mean ± SEM)	51.2 ± 0.2	51.1 ± 0.3	51.5 ± 0.4
Gender (% male)	44.8	49.8	34.3*
Race (% white)	85.1	88.7	77.7*
Hypertension (%)	30.4	24.8	42.2*
Diabetes (%)	6.2	5.0	8.6*
Hypercholesterolemia (%)	26.0	25.4	26.9
Smokers (%)	40.3	38.8	43.5*
History of MI	4.9	3.6	8.6*
Angiographic and hemodynamic			
LV ejection fraction			
Mean ± SEM	69.7 ± 0.2	69.8 ± 0.3	69.6 ± 0.4
<50% (%)	1.6	1.7	2.1*
End-systolic volume index ≥34 ml/m² (%)	13.5	13.1	14.4
End-diastolic volume index ≥90 ml/m² (%)	20.4	19.7	21.7
End-diastolic pressure ≥15 mm Hg (%)	17.6	17.8	17.1
Abnormal contraction (%)	8.1	6.9	10.5*

*$p < 0.01$, +STT versus −STT. Abbreviations as in Table 1.

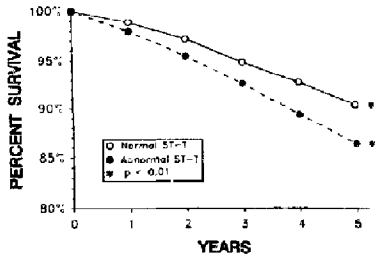

Figure 2. Survival curves depicting the 5-year survival of all patients with and without an ST-T wave abnormality. The two curves are significantly different from each other, indicating a significant effect of ST-T wave changes on survival

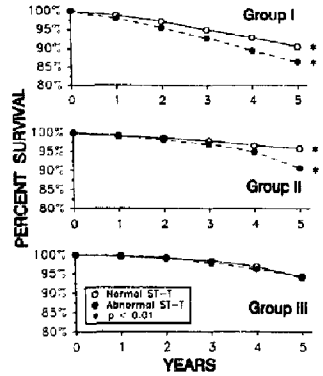

Figure 3. Survival curves depicting the 5-year survival of patients stratified by degree of coronary artery disease and by the presence or absence of an ST-T wave abnormality. Patients in Group I had severe disease (≥70% obstruction of at least one epicardial artery or ≥50% obstruction of the left main artery), those in Group II had mild disease (<70% obstruction of all epicardial vessels and <50% obstruction of the left main artery) and those in Group III had no (<10% obstruction) coronary disease.

follow-up, survival of patients with an ST-T abnormality was 88.3% compared with 92.2% in those without this abnormality ($p < 0.01$).

Survival was also examined in each of the subgroups (Fig. 3). In Group I (patients with severe disease), survival was significantly higher in patients without than in those with an ST-T abnormality. The 5-year survival for patients with severe stenosis and an ST-T abnormality was 86.4% compared with 90.4% for patients with severe stenosis without an ST-T abnormality ($p < 0.01$).

Group I was classified into medically (Group IA) and surgically (Group IB) treated subgroups (Fig. 4). In each subgroup the presence of an ST-T abnormality corresponded to a significantly lower 5-year survival. The medically treated group had a 5-year survival in patients with an ST-T abnormality of 85.6% compared with 87.8% in those without an ST-T change. In the surgically treated group, 88.9% with an ST-T abnormality survived 5 years compared with 93.2% without an ST-T abnormality ($p < 0.01$).

In Group II (patients with mild disease), the 5-year survival was 95.7% in patients without an ST-T abnormality compared with 90.6% in those with an ST-T abnormality (Fig. 3) ($p < 0.01$).

In Group III (patients with no disease), however, there was no significant difference in survival based on the presence or absence of an ST-T abnormality (Fig. 3). The 5-year survival in patients with an ST-T abnormality was 94.3% compared with 94% in those without this abnormality ($p > 0.1$).

Stepwise linear regression analysis. Stepwise discriminant function analyses were performed to determine which demographic, clinical, ECG, hemodynamic and angiographic factors were significant independent predictors of 5-year survival (Table 5).

In patients with severe stenosis treated medically (Group IA), ejection fraction, age and the number of vessels involved were significant predictors of outcome; ejection fraction was the most significant. In the surgically treated group (Group IB), age and ejection fraction were the only significant predictors. ST-T abnormality was not an independently significant predictor of 5-year survival in either subgroup.

In patients with mild coronary stenosis (Group II), age, abnormal left ventricular contraction, left main coronary artery obstruction (<50%) and presence of an ST-T wave abnormality were selected to be independently predictive of 5-year survival. In the subgroup without coronary disease (Group III), age was the only factor selected to be independently predictive of 5-year survival.

Stepwise regression analysis with use of only clinical characteristics. To simulate the clinical situation before catheterization, the analysis was repeated with all the patients in the registry regardless of the degree of coronary artery disease (which would not be known before catheterization) with use of only the clinical characteristics (age, gender, race and history of hypertension, hypercholesterolemia, diabetes, smoking or prior infarction) and the presence or absence of an ST-T abnormality (Table 6). Age, history of myocardial infarction, history of diabetes mellitus, presence of hypertension, history of smoking and presence of an ST-T abnormality were independent predictors of survival.

Effect of left ventricular hypertrophy. The ECG changes of left ventricular hypertrophy commonly coexist with an

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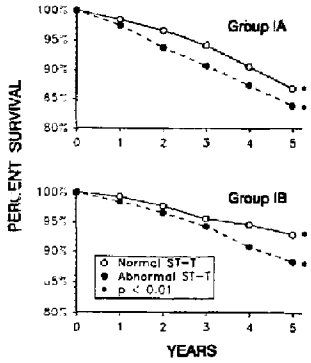

Figure 4. Survival curves depicting the 5-year outcome of patients with severe coronary artery disease (≥70% obstruction of at least one epicardial artery or ≥50% obstruction of the left main artery) stratified by therapy (medical [Group IA] vs. surgical [Group IB]) and presence or absence of an ST-T change.

ST-T abnormality and have been independently related to decreased survival (8). Therefore, the survival analyses were repeated with exclusion of the patients with ECG evidence of left ventricular hypertrophy (n = 693). Diagnosis of left ventricular hypertrophy was based on an age-adjusted point score technique from precordial lead or limb lead amplitudes ($R_I > 1,300\ \mu V$ or $R_{aVL} > 1,100\ \mu V$). There was no difference in the predictors of outcome as compared with those selected when patients with left ventricular hypertrophy were included.

Table 5. Stepwise Discriminant Function Model of Factors Predicting 5-Year Survival

Step	Factor	Standardized Coefficient	p
Group IA (patients with severe obstruction treated medically)			
1	Age	0.722	<0.0001
2	Ejection fraction	−0.582	<0.0001
3	Number of significantly obstructed vessels	0.316	0.0042
Group IB (patients with severe obstruction treated surgically)			
1	Age	0.835	<0.0001
2	Ejection fraction	−0.585	0.0001
Group II (patients with mild coronary obstruction)			
1	Age	0.632	0.0001
2	Abnormal contraction	0.517	0.0014
3	Mild left main stenosis*	0.456	0.0054
4	ST-T abnormality	0.423	0.0091
Group III (patients without coronary obstruction)			
1	Age	1.000	0.0055

*>10% stenosis but <50% stenosis of the left main coronary artery.

Table 6. Stepwise Discriminant Function Model of Factors Predicting 5-Year Survival With Use of Only Clinical Characteristics and the Presence or Absence of an ST-T Abnormality

Step	Factor	Standardized Coefficient	p
1	Age	0.835	<0.0001
2	History of myocardial infarction	0.198	0.0004
3	Diabetes mellitus	0.211	0.0002
4	Hypertension	0.191	0.0006
5	Smoker	−0.169	0.0027
6	ST-T abnormality	0.160	0.0044

Discussion

The ST segment and the T wave are generated by the orderly repolarization of ventricular muscle. During normal ventricular activation, action potentials are shorter in epicardial than in endocardial regions. A transmural gradient of recovery potentials then exists, with extracellular current flowing toward the epicardium producing positive ST-T deflections in overlying epicardial or body surface leads (9,10). Myocardial ischemia, generally more severe in endocardial regions (11), shortens action potential durations; thus, subendocardial action potential durations are shortened to reverse the normal transmural recovery gradient and to produce ST segment depression and T wave inversion (12,13). These changes in systolic injury current are augmented by diastolic injury currents produced by reduced rest potentials in ischemic areas (12,13). A similar effect would be expected with subendocardial infarction.

Relation of ST-T abnormality to coronary artery disease. A relation exists between the prevalence of an ST-T abnormality and coronary artery disease. In general population studies (7,14–16), the prevalence of this ECG abnormality is 7% to 9%. However, in patients suspected of having coronary artery disease, reported prevalences (2,17) are 18% to 24%. Bär et al. (18) reported that 61.2% of patients with angiographically proved coronary artery disease had an ST-T abnormality. In our study groups, the prevalence of ST-T changes varied directly with severity of coronary disease; an ST-T abnormality was found in 51%, 41% and 33% of patients with severe, mild or no disease, respectively.

Subjects with an ST-T abnormality also have different demographic and risk factor patterns than do those without an ST-T change. The findings demonstrated in Tables 1 to 4 are similar to those previously reported. The older age, for example, is consistent with data reported by Rose et al. (19), who documented an almost fourfold increase in the prevalence of ST-T abnormalities in the general population from ages 40 to 69 years, and the higher percent of women is similar to that reported by Liao et al. (16).

Patients with ST-T changes also have more significantly impaired ventricular function than do those with normal repolarization forces for any degree of coronary disease. Previous and current data support this conclusion. O'Keefe et al. (17) showed ST-T changes to be independently correlated with decreasing ejection fraction. Swartz et al. (20) showed that most patients with angiographically proved coronary artery disease and a normal ECG had no evidence of left ventricular asynergy. Previous data (21) have also shown significantly higher angiographic scores in patients with than in those without an ST-T abnormality.

Effects of ST-T abnormality on survival. A reduced survival in patients with an ST-T abnormality has been reported by several investigators (1–5). Connolly et al. (2), for example, studying only patients with suspected coronary artery disease, reported a 76% 5-year survival rate in those with an ST-T abnormality compared with a rate of 87% in those with a normal ECG. Humphries et al. (21) followed up 224 patients with angiographically documented coronary obstruction for 5 to 12 years; in patients with an ST-T abnormality the mortality rate was 26%, compared with a rate of 6.5% in patients with a normal ST-T segment.

It is apparent from our data that a significant number of patients with an ST-T abnormality referred for cardiac catheterization do not have coronary artery disease. In our study 18.8% of all patients with an ST-T abnormality had no disease and another 16.3% had "mild" obstruction. These results support the importance of evaluating angiographically defined patient groups. Otherwise, subsets with different pathophysiologic substrata and different expected outcomes would be combined to confound the analysis of the effect of the ECG change.

As reported here, the role of the ST-T abnormality did indeed differ with the angiographic subset. ST-T changes did affect survival in patients with severe or mild disease, whereas outcome was not affected in those without coronary disease (Fig. 3). This result is consonant with the findings of Humphries et al. (21), who reported that none of their 32 patients with an ST-T abnormality but no angiographically demonstrable coronary disease died in 5 to 12 years of follow-up.

Our data on the direct effect of ECG changes on survival in patients with mild disease extends previous limited information concerning this large and potentially important group. Studies have documented the highly variable flow characteristics of different degrees of coronary stenosis. For example, lesions that reduce cross-sectional area by only 27% may be associated with an impaired reactive hyperemic response, a correlate of physiologic significance (22). Thus, in some patients, a lesion classified angiographically as not significant may be physiologically important.

Although patients with only 50% stenotic lesions are less likely to die than those with ≥75% stenosis (23), a relation between mild disease and subsequent infarction has also been demonstrated. Little et al. (24) and others (25) reported that an acute occlusion leading to acute infarction commonly develops in vessels that were previously demonstrated to have ≤50% obstruction. Thus, these "mild" lesions may have clinical as well as physiologic significance.

Correlates of reduced survival. The decreased survival associated with an ST-T abnormality may represent any of several effects. The observed ECG abnormality may be a marker for other factors that are the primary determinants of survival. Thus, ST-T abnormalities may reflect more extensive coronary atherosclerosis with or without more severe left ventricular dysfunction, both of which are known to decrease survival time (6,7). Prior studies have demonstrated such a relation between ST-T abnormalities and extent of disease (21) and left ventricular dysfunction (17,20). However, the ECG findings may have no independent significance.

The plausibility of this hypothesis in patients with severe disease is suggested by the differences in clinical and pathophysiologic characteristics of patients with and without ST-T changes (Tables 1 to 4) and is supported by the results of stepwise regression analysis (Table 5). Only variables that are independent, significant correlates of survival are selected by the model. Ejection fraction, age and the number of diseased vessels were selected in the medically treated group and ejection fraction and age were selected in the surgically treated group as correlates of 5-year survival. These variables have all been previously shown to predict mortality in patients with coronary disease in general and after surgical therapy (6,7).

ST-T abnormality was not selected as a variable. Thus, even though patients with ST-T changes did have reduced survival (Fig. 2 to 4), ST-T changes were not an independent predictor of survival in either the medically or the surgically treated subgroup. The effect of the ECG change is thus mediated through its significant relation to other variables—ventricular function, extent of disease and age—that are the primary or direct determinants of outcome.

However, in patients with mild disease, the regression model did identify ST-T changes—in addition to age, abnormal ventricular contraction and mild left main coronary disease—as independent predictors of survival. Thus, ST-T changes are a direct and independent determinant of increased mortality beyond that provided by other variables. In this group of patients, the presence of an ST-T wave abnormality may identify a subset in which the angiographically mild lesion is physiologically important. This may occur as a result of increased arrhythmogenesis, with ST-T abnormalities reflecting disordered ventricular recovery properties that are a precedent for ventricular fibrillation (26,27).

Finally, in patients with no disease, age was the only factor chosen to independently correlate with 5-year survival; ST-T abnormality did not appear. This was to be expected from the absence of an effect of ECG changes in a univariate analysis (Fig. 3).

These factors remained active after patients with left ventricular hypertrophy were excluded. This exclusion was

based on ECG criteria that are known to have limited sensitivities or specificities, or both. Results may have differed if anatomic criteria for hypertrophy were used or if other ECG standards were relied upon.

Applications before cardiac catheterization. The analyses we have described presuppose knowledge of coronary anatomy and left ventricular function when assessing the prognostic value of the ST-T wave abnormalities. However, these important data are not available when the physician first encounters the patient or in studies in which cardiac catheterization is not routinely performed. To simulate these conditions, the analysis was repeated using all patients regardless of the degree of coronary artery stenosis as cases and only clinical characteristics as independent variables. Under these conditions, ST-T abnormality was selected as an independent predictor of 5-year survival (Table 6,. This is in agreement with data from the Framingham study (5) and others that showed ST-T abnormality to be independently correlated with survival in the general population.

Conclusions. The data presented here suggest that an ST-T abnormality affects survival in the presence of mild to severe coronary artery disease but not in the absence of such disease. In patients with mild disease, the abnormality has significance independent of clinical, hemodynamic and angiographic data in predicting 5-year survival. However, when coronary artery disease is severe, it no longer adds independent significance.

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