

# Outcome in Medically Treated Coronary Artery Disease

## Ischemic Events: Nonfatal Infarction and Death

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**SUMMARY** In this study we extended the characterization of outcome in 1214 medically treated patients with coronary disease by considering nonfatal infarction and death together as ischemic events. At 7 years, the cumulative event rate was 47% (18% for nonfatal infarction as the initial event and 29% for death as the initial event). In multivariable analysis of 81 baseline descriptors, 11 (six clinical and five catheterization) were independent predictors of events. Progressive chest pain, number of diseased vessels, left main stenosis and left ventricular (LV) function were the most important predictors. Progressive pain was a more important predictor of total events than of survival alone. In patients with one-, two- or three-vessel disease and normal LV function, nonfatal infarction accounted for at least 50% of initial events. In patients with left main disease or severe LV dysfunction, death was the predominant event. These results have important implications for interpreting the natural history of coronary artery disease.

A MAJOR FOCUS of this laboratory has been the characterization of the natural history of coronary artery disease. In a recent report,<sup>1</sup> we described natural history in terms of survival in a group of 1214 symptomatic medically treated patients. This description included an analysis of the prognostic importance of 81 baseline variables. The goal of the present report was to extend the characterization of the natural history to include nonfatal myocardial infarction.

Other authors<sup>2-11</sup> have used two approaches to investigate the incidence of nonfatal infarction in medically and surgically treated patients with coronary artery disease. One approach considers myocardial infarction and death as independent events.<sup>2, 3, 5-10</sup> The other approach considers nonfatal infarction and death together as related ischemic events.<sup>4, 10, 11</sup> Nonfatal infarction and death are not clinically independent events, so we describe natural history or outcome in terms of total ischemic events, nonfatal myocardial infarction and death.

The specific objectives of this study were (1) to document the incidence of initial events after catheterization in 1214 symptomatic medically treated patients with coronary disease; (2) to identify, by mul-

tivariable analysis, which of 81 baseline characteristics were significant independent predictors of events; and (3) to examine the incidence of events, including the relative incidence of fatal and nonfatal events, in clinically important subsets defined by the important predictors.

In a subsequent report, we will investigate factors that distinguish fatal from nonfatal events.

### Methods

#### Patient Population

The patients included 1214 symptomatic, medically treated subjects with significant coronary disease. The group was identical to the population recently examined to identify independent predictors of survival.<sup>1</sup> This population was drawn from 2123 consecutive patients catheterized at Duke University Medical Center between November 1969 and January 1978 who were found to have significant coronary disease. Significant disease was defined as 75% or greater luminal diameter narrowing of one or more major coronary arteries.<sup>12</sup> One hundred thirty patients without chest pain at the time of catheterization and 779 surgically treated patients with chest pain were excluded. The pain-free patients were excluded because they were a heterogeneous group catheterized for a variety of reasons, including complications of acute myocardial infarction, severe heart failure and intractable arrhythmias.

Medical therapy routinely consisted of dietary advice and risk factor modification. Short-acting nitrates were used throughout the study for relief of anginal symptoms. From their earliest introduction, long-acting nitrates and  $\beta$ -blocking agents were also used aggressively for treatment of angina.

#### Patient Selection

Decisions concerning catheterization and selection of therapy were made by physicians in conjunction

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with their patients. All physicians had access to the clinical information system described below and could readily review disease prevalence or clinical outcome in specific patient groups of interest. Because of the nature of the decisions and varying practices of the physicians, precise criteria for patient selection cannot be quoted.<sup>13</sup> Most patients were catheterized because of the severity of their symptoms; some were catheterized to determine their coronary anatomy and ventricular function and others were catheterized to exclude left main coronary artery disease. In general, except in patients with left main disease, incapacitating angina was the main indication for surgery. Although some patients were treated medically because they were anatomically and/or hemodynamically unsuitable for surgery, most were suitable for surgery but were not operated on after the information acquired at catheterization, the severity of symptoms and the response to treatment were considered.

#### Baseline Information

The computerized information system used for this study has been described in detail.<sup>1, 14</sup> In summary, a baseline data set consisting of multiple noninvasive clinical descriptors and catheterization variables was collected and stored prospectively for each patient at the time of catheterization. The baseline characteristics analyzed in this study consisted of the same 57 clinical noninvasive characteristics and 24 catheterization descriptors that were previously analyzed with respect to survival.<sup>1</sup>

The noninvasive characteristics consisted of descriptors of the history, physical examination, chest x-ray and ECG. Chest pain was characterized according to its frequency, time of occurrence, severity, type, and course in the 6 weeks preceding catheterization. Progressive chest pain was defined as a clinical increase in the severity or frequency of pain in the 6 weeks preceding catheterization. Spontaneous chest pain accompanied by documented, reversible, ST-segment elevation was characterized as variant angina.

The catheterization variables consisted of hemodynamic, angiographic and ventriculographic descriptors. Coronary angiograms were performed in multiple left anterior oblique (LAO) and right anterior oblique (RAO) projections. They were interpreted in conference by at least two of the same three experienced angiographers. Lesions estimated to be causing 50% or less narrowing of the luminal diameter were classified as insignificant. Lesions estimated to be causing approximately 75% or more narrowing were classified as significant. When disagreement arose as to whether a lesion was significant or insignificant, it was measured and assigned to the appropriate category.

Biplane left ventriculography was performed in simultaneous shallow RAO and steep LAO projections. The left ventricular (LV) contraction pattern was interpreted as abnormal if there were one or more

areas of localized asynergy defined as hypokinesis, akinesis, dyskinesis or a combination of the three. The sites of localized asynergy were characterized as anterior, apical or inferior. Abnormal ventricular contraction was also characterized as diffusely abnormal if there were multiple areas of asynergy that produced a diffusely abnormal contraction pattern with an estimated ejection fraction of less than 25%.

#### Follow-up

Follow-up information was obtained 6 and 12 months after cardiac catheterization and annually thereafter by a staff cardiologist during a clinic visit or by a research associate by telephone. Overall, the follow-up was 99% complete. At each interval, functional status was ascertained and interval hospitalizations were documented. When there was a possibility that an ischemic event had occurred, the patient's physician was contacted and asked to confirm the diagnosis for each event and to provide relevant discharge summaries and documentation. Evidence of enzyme and electrocardiographic changes was obtained for fatal and nonfatal myocardial infarction, as was a description of the cause and circumstances of all deaths.

Myocardial infarction was defined as the occurrence of a characteristic clinical history in association with one of the following criteria: (1) the appearance of new 0.04-second Q waves on the ECG; (2) a typical evolutionary pattern of ST-T-wave changes accompanied by a transient elevation of total creatine kinase (CK), or if CK was not measured, appropriately timed elevations of serum glutamic oxaloacetic transaminase (SGOT) or lactic dehydrogenase (LDH); or (3) if ECGs could not be obtained, or changes were uninterpretable (e.g., left bundle branch block), a transient elevation of CK (or SGOT or LDH if CK was not measured), accompanied by positive isoenzyme changes (the appearance of an MB band of CK or reversal of the LDH1:LDH2 ratio). An infarct was defined as nonfatal if the patient was discharged from hospital. The criteria for myocardial infarction were liberal to ensure that all episodes were recorded. However, only four myocardial infarctions were diagnosed by enzyme evidence alone, and these were in patients for whom ECGs could not be obtained. In another seven patients, no ECG or enzyme documentation could be obtained, but the patient's physician confirmed that a positive diagnosis of infarction had been made. These seven patients were also included as having suffered an infarct.

#### Verification of Nonfatal Infarct Information

Despite a low threshold for recognizing nonfatal infarction, failure to detect infarcts remained the most likely error. To access the error rate, we contacted 520 high-risk patients (medical and surgical survivors with three-vessel disease) by letter, requesting details of chest pain and hospitalization since catheterization.

Physicians were contacted about previously unrecorded ischemic events. Among 362 patients who replied, only one previously unrecorded nonfatal infarct was detected. Because the response to the letter survey was lower than the telephone follow-up rate, we instituted a secondary check. The entire course since catheterization has been reviewed in approximately 300 patients who have returned to the follow-up clinic in the last 12 months. No unsuspected infarcts have been detected by this mechanism.

### Data Analysis

Cumulative survival rates from the time of catheterization were calculated by standard life-table methods.<sup>15</sup> The cumulative initial event rate, the complement of the event-free rate,<sup>4, 11, 16</sup> was calculated by treating nonfatal infarction and death as terminating events. The two components of the initial event rate, the rate at which death occurred as an initial event (the initial death rate), and the rate at which nonfatal infarction occurred as an initial event (the nonfatal infarct rate) were calculated individually from the probability of reaching a given interval event-free and of having the event in that interval. The initial death rate and the nonfatal infarct rate calculated individually, summed to the initial event rate. Because the initial death rate included only deaths that occurred without a preceding infarction, it was lower than the overall mortality rate if patients died after a nonfatal infarction.

Breslow's formulation<sup>17</sup> of the Cox proportional hazards model<sup>18</sup> was used to determine the relationship between baseline characteristics and the incidence of cardiac events. The dependent variable was the time from catheterization to the first event. An unadjusted (univariate) chi-square statistic was calculated for each of the 81 characteristics. This statistic represented the relationship between a characteristic and cardiac events without adjustment for the effects of other characteristics. To determine

which characteristics were significant independent predictors of cardiac events, all 81 baseline characteristics were analyzed jointly with the Cox model by a stepwise strategy similar to that proposed by Bartolucci and Fraser.<sup>19</sup> This procedure has been described elsewhere.<sup>1</sup>

One hundred twenty-seven patients who first were treated medically and later underwent surgery were included in the analyses until their date of operation, when they were withdrawn (censored) alive.

### Results

#### Incidence of Events in the Total Group

The outcome of the group of 1214 patients is shown in table 1. There were 245 cardiovascular deaths and 14 noncardiovascular deaths. Cardiovascular death was the first event after catheterization in 217 patients. Nonfatal infarction was the first event after catheterization in 133 patients, of whom 28 later died. Eighty-one of the initial nonfatal infarcts were transmural and 41 were nontransmural. The extent of infarction could not be determined in the 11 patients in whom ECGs were not obtained.

The cumulative event rates are illustrated in figure 1. The cumulative initial event rates at 1, 5 and 7 years were 14%, 36% and 47%, respectively. The corresponding nonfatal infarct rates were 6%, 14%, and 18%, respectively, and the corresponding initial death rates were 8%, 22% and 29%, respectively. Nonfatal infarction accounted for 38% of the initial event rate at 7 years. Because 28 patients died after an initial nonfatal infarct, the overall mortality rates of 9%, 27% and 35% at 1, 5 and 7 years were slightly higher than the corresponding initial death rates.

#### Independent Predictors of Cardiac Events

Fifty of the 81 baseline characteristics were significant ( $p < 0.05$ ) univariate predictors of ischemic events. When all 81 characteristics were analyzed

TABLE 1. Interval Outcome Data for the Total Group of 1214 Medically Treated Patients with Significant Coronary Disease

	Followed	Event-free	Death (initial event)	Nonfatal infarct*	Withdrawn†
0	1214	—	—	—	—
6 mo	1214	1080	73	53	8
1 yr	1080	997	28	18	37
2 yr	997	733	42	25	197
3 yr	733	531	27	16	159
4 yr	531	388	21	7	115
5 yr	388	269	9	8	102
6 yr	269	157	9	2	101
7 yr	157	73	5	4	75
8 yr	73	19	3	0	51
9 yr	19	2	0	0	17

\*Twenty-eight patients who initially suffered a nonfatal infarct later died.

†Patients who had not reached their anniversary date, were lost to follow-up, died of noncardiovascular causes or crossed over to surgery.

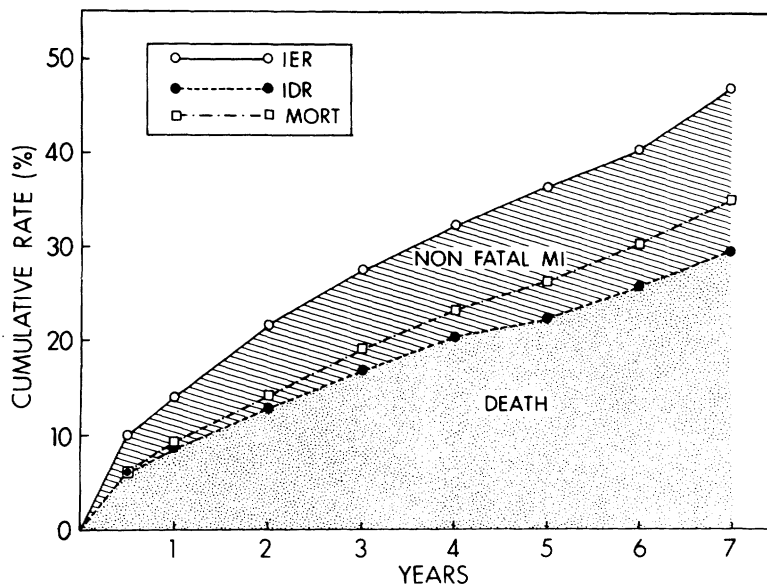


FIGURE 1. Cumulative event rates in 1214 medically treated patients with coronary disease, catheterized because of chest pain. IER = initial event rate; IDR = initial death rate; MORT = mortality rate; MI = myocardial infarction. At any interval, the nonfatal infarct rate equals the difference between IER and IDR.

jointly with the Cox model, only 11 characteristics, six clinical and five catheterization, were independently significant predictors of events. They are listed in table 2 in the order in which they were selected by the stepwise procedure. The interpretation of this order is that the first variable chosen is the descriptor with the strongest relationship to outcome; the second, when added to the first, gives the best pair of variables for predicting outcome, and so on. For example, the best combination of four variables for predicting outcome

comprised New York Heart Association (NYHA) class IV heart failure, number of diseased vessels, progressive chest pain and variant angina. The chi-square statistics reported in table 2 are based on the final combination and provide a measure of the influence of each characteristic, after adjusting for all other variables selected. The magnitude of these statistics does not necessarily coincide with the order in which variables were chosen, because the independent contribution of any variable may be influenced by variables chosen later in the stepwise process.

TABLE 2. Significant Independent Predictors of Cardiac Events (Nonfatal Infarction and Death)

Characteristic	Adjusted chi-square
NYHA class IV heart failure	9.93
Number of diseased vessels	14.49
Progressive chest pain	19.75
Variant angina	14.42
Diffusely abnormal LV contraction	7.19
Significant left main stenosis	11.28
History of peripheral vascular disease	10.86
Resting ST-T-wave abnormalities	7.09
Anterior LV contraction abnormality	9.13
Arteriovenous oxygen difference	10.26
Nocturnal chest pain	6.79

Variables are listed in the order in which they were selected by the stepwise procedure. Adjusted chi-square statistics were computed with all the above variables considered together.

Chi-square > 6.63 corresponds to  $p < 0.01$ ; chi-square > 10.81 corresponds to  $p < 0.001$ .

The total chi-square for all 11 variables ( $-2 \log$  likelihood ratio) was 267.24, with  $p < 0.00001$  when judged with 81 degrees of freedom. This indicates that obtaining 11 significant variables from 81 candidates is not just a spurious finding.

Abbreviations: NYHA = New York Heart Association; LV = left ventricular.

### The Incidence of Events in Relation to Independent Predictors

#### Clinical Characteristics

**Chest pain descriptors.** Chest pain descriptors were important independent predictors of ischemic events. The 5-year initial event rate was 48% in 461 patients with progressive chest pain, compared with 29% in 753 patients with nonprogressive pain (fig. 2). The increased event rate associated with progressive pain was due to a higher nonfatal infarction rate (19% vs 11% at 5 years) and a higher initial death rate (29% vs 18% at 5 years). The event rates in patients with progressive pain were further elevated if they also suffered from nocturnal pain. The 5-year initial event rate in 283 patients whose chest pain was progressive and nocturnal was 57%. The corresponding nonfatal infarct and initial death rates were 22% and 35%, respectively. In patients who did not have progressive pain, the occurrence of nocturnal pain did not affect the event rates. Twenty-three patients had variant angina; nine of them suffered nonfatal infarction and three died within 6 months of catheterization.

**Class IV heart failure and ST-T-wave changes.** In contrast to chest pain descriptors, NYHA class IV heart failure and resting ST-T-wave changes predominantly affected the death rate. Of 35 patients with NYHA class IV heart failure, 28 died within 3

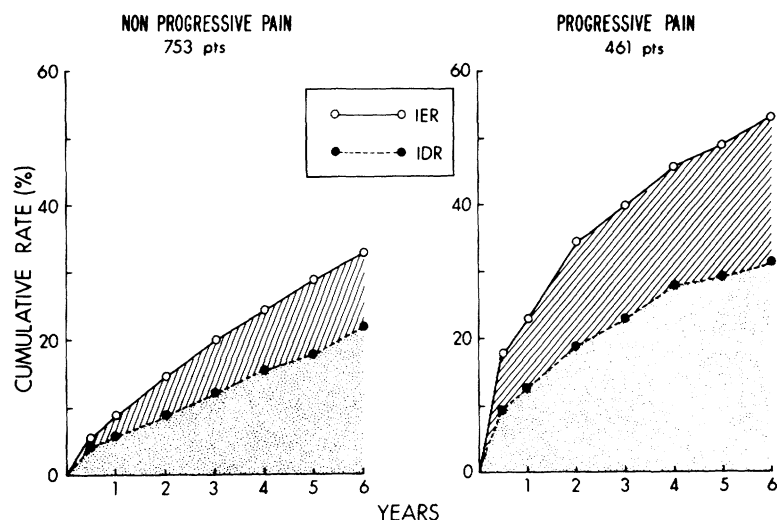


FIGURE 2. Cumulative event rates and pattern of chest pain. IER = initial event rate; IDR = initial death rate.

years, 26 without preceding nonfatal infarction and two after nonfatal infarction. The 5-year initial event rate was 43% in 583 patients with abnormal resting ST-T waves, compared with 29% in 631 patients with normal ST-T waves. The corresponding nonfatal infarct and initial death rates were 14% and 29% in patients with abnormal ST-T waves, compared with 13% and 16% in patients with normal ST-T waves.

**Peripheral vascular disease.** Fifty-seven patients had a history of peripheral vascular disease, which was defined as a clinical history of claudication or previous surgery for aorto-ilio-femoral obstructive disease. The 3-year initial event rate was 52% in patients with a history of peripheral vascular disease, compared with 26% in patients without peripheral vascular disease. The corresponding nonfatal infarct and initial death rates were 18% and 34% in patients with peripheral vascular disease, compared with 10% and 16% in patients without peripheral vascular disease.

#### Catheterization Variables

**Coronary anatomy.** The number of significantly stenosed vessels and the presence of significant left main stenosis were independent predictors of cardiac events. The relationship between initial events and coronary anatomy is illustrated in figure 3. Five-year initial event rates were 18% in one-vessel disease (307 patients), 28% in two-vessel disease (309 patients), 46% in three-vessel disease (521 patients) and 70% in left main coronary artery disease (77 patients). In the progression from one- to three-vessel disease, the 5-year nonfatal infarct rate increased from 12% to 16%; but there was a much larger increase in the initial death rate, from 6% to 30%. Patients with left main stenosis had the lowest 5-year nonfatal infarct rate (9%) but the highest initial death rate (61%). In one- and two-vessel disease, nonfatal infarction accounted for 67% and 50%, respectively, of the initial event rate at 5 years, whereas in three-vessel and left main disease, nonfatal infarction accounted for only 35% and 13%, respectively, of the initial event rate at 5 years.

**LV function.** Two descriptors of LV contraction

pattern and one hemodynamic descriptor (arteriovenous oxygen difference) were significant independent predictors of initial events. To simplify the description of ventricular function and allow comparison with previously reported survival results, the event rates are illustrated in relation to the LV contraction pattern (fig. 4). Patients with an abnormal, but not diffusely abnormal contraction pattern, were considered to have moderate LV dysfunction. They were further subdivided according to the presence or absence of anterior wall asynergy. Patients with a

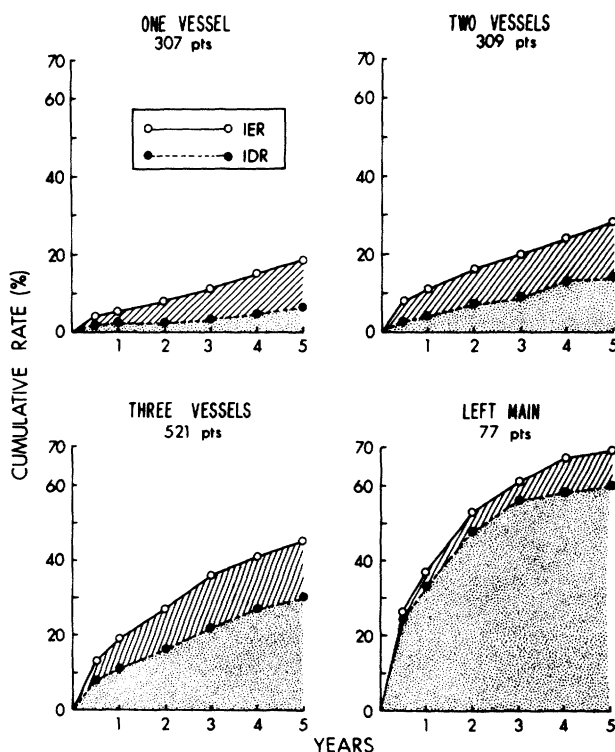


FIGURE 3. Cumulative event rates and coronary anatomy. IER = initial event rate; IDR = initial death rate.

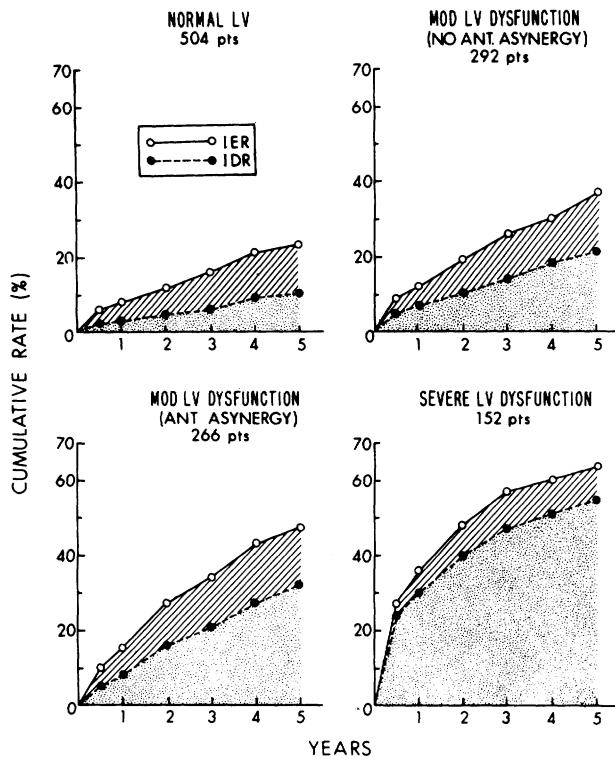


FIGURE 4. Cumulative event rates and left ventricular (LV) function. Moderate LV dysfunction = abnormal but not diffusely abnormal contraction; severe LV dysfunction = diffusely abnormal contraction; IER = initial event rate; IDR = initial death rate.

diffusely abnormal contraction pattern were considered to have severe LV dysfunction.

The initial event rate increased markedly with increasing impairment of ventricular function. At 5 years, it ranged from 23% in 504 patients with normal LV contraction to 64% in 152 patients with severe LV

dysfunction. The increase in the initial event rate was associated with a consistent increase in the death rate. There was no consistent relationship between the nonfatal infarct rate and LV function, although the nonfatal infarct rate was lowest in patients with severe LV dysfunction (9% at 5 years). At 5 years, nonfatal infarction accounted for 56% of the initial event rate in patients with normal LV function, 43% and 32% of the initial event rate in the two categories of patients with moderate LV dysfunction and 14% of the initial event rate in patients with severe LV dysfunction.

Event rates of patients with one-, two- and three-vessel disease and normal or moderately impaired LV function are illustrated in figure 5. Again, the initial event rate and the initial death rate tended to increase with increasing anatomic involvement and worsening ventricular function. The 5-year nonfatal infarct rate in patients with normal LV function showed a small increase, from 9% in one-vessel disease to 14% in three-vessel disease; otherwise, there was no consistent pattern.

With increasing anatomic involvement and worsening ventricular function, nonfatal infarction accounted for a decreasing proportion of the initial events. However, in patients with normal LV function, nonfatal infarction accounted for at least half of the 5-year initial event rate: 69%, 68% and 50% in one-, two- and three-vessel disease, respectively. In patients with moderate LV dysfunction and one-, two- or three-vessel disease, nonfatal infarction accounted for 62%, 54% and 37% of the 5-year initial event rate.

#### Combined Clinical and Catheterization Variables

The relationship between cardiac events, progressive chest pain and ventricular function is illustrated in figure 6 for patients with three-vessel disease. At each level of ventricular function, progressive

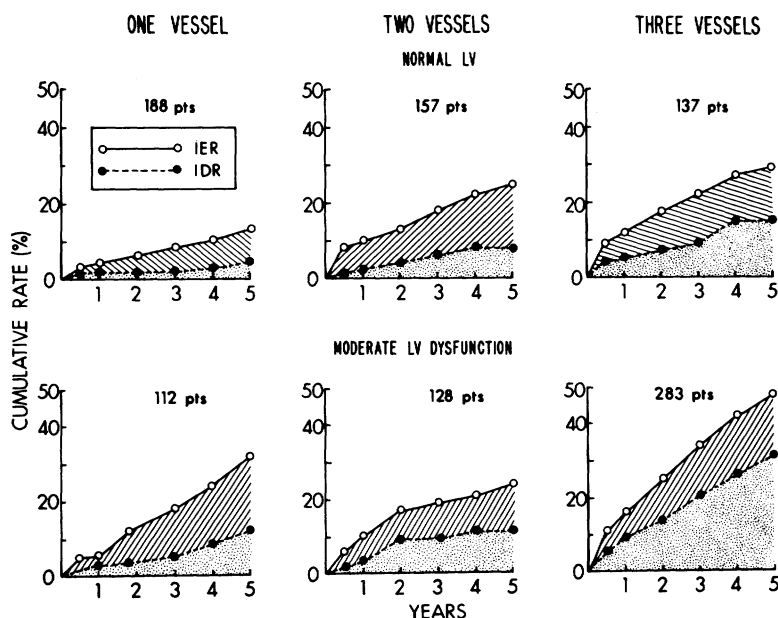


FIGURE 5. Cumulative event rates related to coronary anatomy and ventricular function. LV = left ventricular; IER = initial event rate; IDR = initial death rate.

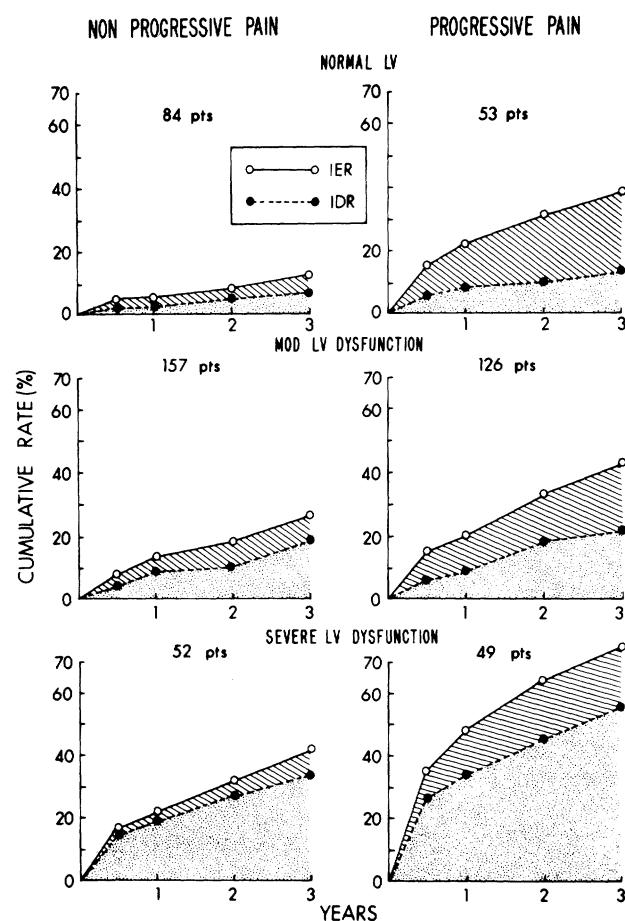


FIGURE 6. Cumulative event rates and progressive chest pain at each level of ventricular function in patients with three-vessel disease. LV = left ventricular; IER = initial event rate; IDR = initial death rate.

pain was associated with an increased incidence of ischemic events. The increase was largest in patients with normal LV function, where the 3-year event rate was 38% in 53 patients with progressive pain, compared with 12% in 84 patients with nonprogressive pain. At each level of ventricular function, the increase in event rate was due to an increase in both the nonfatal infarction rate and the initial death rate. At each level, the 3-year nonfatal infarct rate associated with progressive pain was at least twice that associated with nonprogressive pain. In patients with normal LV function, the 3-year nonfatal infarct rate was 24% in patients with progressive pain and 5% in patients with nonprogressive pain. The effects of progressive chest pain in one- and two-vessel disease were essentially the same as in three-vessel disease.

### Discussion

The results of this study agree with previous reports<sup>2, 5, 6, 9-11, 20-22</sup> concerning the frequency of nonfatal myocardial infarction in the clinical course of coronary artery disease. With nonfatal infarction included as an end point, the incidence of total ischemic

events in several subsets of patients is far greater than is appreciated when survival alone is considered. Nonfatal infarction accounted for approximately one-third of the initial cardiac events after catheterization in the total group of 1214 patients. However, in patients with one- or two-vessel disease and normal ventricular function, nonfatal infarction accounted for as much as two-thirds of the initial events. Even in patients with three-vessel disease and normal ventricular function, approximately half of the initial events were nonfatal infarctions. When survival alone is considered in these categories, a significant proportion of the ischemic events are overlooked.

In general, the results are comparable to early studies of uncatheterized patients with clinically diagnosed coronary disease. In an international cooperative study of 241 patients with coronary heart disease,<sup>20</sup> there were 41 deaths and 14 nonfatal first infarctions over 5 years. In the Framingham study,<sup>21</sup> the probability of a coronary attack within 8 years after onset of angina in men over 45 years was about 50%. In the Health Insurance Plan (HIP) study of 275 men followed for 30 months,<sup>22</sup> the incidence of infarction (12.5%) was higher than the incidence of death (7.5%). People who had suffered previous infarction were excluded from the HIP study. In the equivalent patients in the present study, those with relatively normal ventricular function, nonfatal infarction was also usually more frequent than death as an initial event.

In a Cleveland Clinic series of 590 patients with angiographically proved coronary disease followed 5-9 years,<sup>2</sup> there were 244 deaths and 38 nonfatal infarcts among the survivors. Because of difference in definitions, patient selection and subsequent exclusions, we do not believe the results of the Cleveland series and our own can be meaningfully compared.

Several groups<sup>23-26</sup> have recently reported annual mortalities of 4% or less over 2-3 years in medically treated patients with multivessel disease and normal LV function. Our own experience<sup>1</sup> has been similar over a slightly longer follow-up (5-year survival: 90% and 82% in two- and three-vessel disease with normal LV function). Although these patients with multivessel disease and normal LV function have recently been characterized as having a "good prognosis,"<sup>27</sup> the finding that they experience nonfatal infarction at the same rate as death has influenced our perspective of their natural history. Nonfatal infarction may drastically alter a patient's prognosis.<sup>28</sup> Thus, within the group of patients with normal LV function, a continuing, relatively high rate of nonfatal infarction is likely to maintain or even increase the mortality rate over a long follow-up period. Thus, improving the long-term survival rate in patients with multivessel disease and good ventricular function may depend on decreasing the incidence of nonfatal ischemic events.

The fact that there were 11 significant independent predictors of total outcome confirms our previous conclusion that the natural history of coronary disease cannot be defined without reference to multiple clinical and catheterization baseline characteristics.<sup>1</sup> Not unexpectedly, there is some overlap between the



factors that predict events and those that predict death; but there are also marked differences. The most striking difference is in the relative importance of the various predictors. Ventricular function, a potent predictor of survival,<sup>1</sup> appears to be a less important predictor of total events. The number of diseased vessels, also an important predictor of survival,<sup>1</sup> appears to be a relatively more important predictor of total events. However, when total events are considered, chest pain descriptors are among the most important predictors of outcome in patients with coronary disease.

Progressive pain increased the incidence of fatal and nonfatal events at all levels of ventricular function in patients with three-vessel disease. In those with normal ventricular function, the increase in nonfatal events predominated, whereas in those with severely impaired ventricular function, the increase in fatal events predominated. The shape of the event rate curves indicates that progressive pain exerts most of its effect in the 12 months or so after catheterization. Other authors have shown that variant angina is closely associated with impending myocardial infarction.<sup>29, 30</sup> This study confirms that variant angina is an independent predictor of total events and illustrates its importance within the hierarchy of prognostically important factors in coronary disease.

We believe that the results of our recent studies of outcome in medically treated patients with coronary artery disease can be summarized to provide an interpretation of the natural history of coronary artery disease. The clinical course of the disease can be viewed as a series of ischemic events. The degree of anatomic involvement and, to a slightly lesser extent, the degree of impairment of ventricular function appear to be important determinants of the frequency of ischemic events. Progressive chest pain and variant angina are important short-term predictors of the likelihood of an event, possibly because these pain patterns are manifestations of a critical myocardial oxygen demand/supply situation. The probability of surviving an ischemic event is strongly influenced by the quality of LV function and the presence of left main stenosis. In the absence of left main disease, baseline ventricular function is the most important predictor of survival over a short follow-up period. Over longer periods, the extent of anatomic involvement and its progression and the pattern of chest pain during follow-up are likely to emerge as the most important predictors of survival because these factors are associated with the incidence of nonfatal infarction. This interpretation of the natural history of coronary disease will not be a new concept to many clinicians who have come to similar conclusions from their own experience. This report provides quantitative support for such an interpretation.

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## Noninvasive Prediction of Multivessel Disease After Myocardial Infarction

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**SUMMARY** In 65 patients with a previous transmural myocardial infarction (anterior in 33, inferior in 32), exercise thallium scanning was compared with 12-lead exercise electrocardiography to see if multivessel disease could be detected. At coronary arteriography 40 patients were shown to have multivessel disease ( $\geq 70\%$  diameter stenosis in two or three vessels) and 25 patients had one-vessel disease. On the exercise scan thallium defects corresponding to the electrocardiographic site of infarction were present in all patients.

Patients with one-vessel and multivessel disease were separated by exercise-induced angina, perfusion defects on the exercise thallium scan in more than one specific vascular area, and a positive exercise ECG associated with angina, but not by a positive exercise ECG alone. Of the 40 patients with multivessel disease, 85% had defects in more than one vascular area on the thallium scan and 70% had a positive exercise ECG ( $p = \text{NS}$ ). Of the 37 patients with thallium defects in more than one specific vascular area, 92% had multivessel disease, compared with 72% of the 39 patients who had a positive exercise ECG ( $p < 0.05$ ).

Periinfarctional ischemia was present in 38 of the 65 patients (58%) (14 of 25 with one-vessel disease and 24 of 40 with multivessel disease), and did not correlate with the severity of the corresponding coronary artery disease. When thallium defects that resolved were noted in a second vascular area, they were associated with a resolving rather than a constant defect in the vascular area where the infarction had occurred ( $p < 0.005$ ).

In patients after a transmural myocardial infarction, multivessel disease can be better differentiated from one-vessel disease by thallium scanning than by exercise electrocardiography.

**PROGNOSIS** after myocardial infarction depends on the extent of coronary artery disease.<sup>1,2</sup> A positive stress ECG after myocardial infarction is reported to predict multivessel disease with a sensitivity of 41–91%.<sup>3–5</sup> Comparative studies of thallium-201 myocardial perfusion scanning and electrocardiography have shown thallium scanning to be more sensitive in detecting coronary artery disease.<sup>6–8</sup>

In this study exercise electrocardiography and exercise thallium-201 myocardial scanning were compared and related to coronary arteriographic findings in patients with a previous transmural myocardial infarction to see if one-vessel and multivessel disease could be differentiated.

### Methods

Sixty-five patients (63 males and two females) with ECG evidence of a single previous transmural myocardial infarction defined according to the Q-wave criteria of the American Heart Association<sup>9</sup> underwent exercise stress testing with thallium-201 myocardial perfusion scanning 3–72 months after infarction (mean 30 months). The mean age of the patients was 50.4 years (range 32–64 years). Fifty-one of the 65 patients complained of angina pectoris after the myocardial infarction, and 42 of the 65 (65%) were taking  $\beta$  blockers.

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