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## PROGNOSTIC IMPORTANCE OF MYOCARDIAL ISCHEMIA DETECTED BY AMBULATORY MONITORING EARLY AFTER ACUTE MYOCARDIAL INFARCTION

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**Abstract Background.** After an acute myocardial infarction, it is important to determine the risk of a subsequent coronary event. We studied the prognostic value of myocardial ischemia detected by ambulatory electrocardiographic (ECG) monitoring in patients who had recently had an acute myocardial infarction.

**Methods.** Five to seven days after acute myocardial infarction, 406 patients underwent 48-hour ambulatory ECG monitoring, with submaximal exercise testing before discharge and measurement of the left ventricular ejection fraction within 28 days after infarction. Death, nonfatal myocardial infarction, and admission to the hospital because of unstable angina were the principal end points recorded during the one-year follow-up period.

**Results.** The overall incidence of myocardial ischemia detected by ambulatory ECG monitoring was 23.4 percent. The mortality rates at one year were 11.6 percent among the patients with ischemia and 3.9 percent among those without ischemia ( $P=0.009$ ); 3.9 percent among the patients with a positive exercise test, 3.0 percent among those with a negative exercise test, and 16.4 percent among those in whom an exercise test was not performed ( $P<0.001$ ); and 3.6 percent among the patients with an ejection fraction greater than 50 percent, 3.5 percent among those with an ejection fraction be-

tween 35 and 50 percent, and 18.2 percent among those with an ejection fraction below 35 percent ( $P=0.001$ ). Using multiple logistic regression, we found that no diagnostic test performed after myocardial infarction provided additional prognostic information beyond that provided by the standard clinical variables used to predict the risk of death. When nonfatal myocardial infarction and admission to the hospital because of unstable angina were also included as outcome variables, ambulatory monitoring for ischemia was the only test that contributed significantly to the model. For the patients with ischemia detected by ambulatory monitoring, as compared with those who did not have evidence of ischemia, the odds ratio was 2.3 (95 percent confidence interval, 1.2 to 4.5) for death or nonfatal myocardial infarction ( $P=0.009$ ) and 2.8 (95 percent confidence interval, 1.6 to 4.8) for death, nonfatal myocardial infarction, or admission to the hospital because of unstable angina ( $P<0.001$ ).

**Conclusions.** Myocardial ischemia detected by ambulatory ECG monitoring is common early after acute myocardial infarction and provides prognostic information beyond that available from standard clinical information. (N Engl J Med 1996;334:65-70.)

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**S**URVIVORS of acute myocardial infarction are at increased risk for death, recurrent infarction, and unstable angina for many months. Assessing the risk of these events is an important component of subsequent management. The exercise test is the most commonly used diagnostic test for the detection of residual myocardial ischemia. Approximately 30 percent of patients undergoing exercise testing soon after myocardial infarction have an ST-segment depression.<sup>1-7</sup> The mortality at one year in this group of patients may be as high as 27 percent (range, 3 to 27 percent). A substantial proportion of patients cannot exercise, and this group includes patients at high risk for subsequent cardiac events.<sup>8,9</sup> Submaximal exercise testing is usually performed at the time of discharge from the hospital and

may be less predictive than maximal stress testing performed later.<sup>10</sup>

Current data indicate that myocardial ischemia detected by ambulatory electrocardiographic (ECG) monitoring may be a strong predictor of subsequent cardiac events in patients with coronary artery disease.<sup>11-24</sup> The strength and generalizability of the available evidence are limited by small samples,<sup>15,16,22</sup> narrow eligibility criteria,<sup>15</sup> and retrospective data collection.<sup>14,15,18</sup> The prognostic value of ischemia detected by ambulatory ECG monitoring and its relation to the results of exercise testing in patients soon after acute myocardial infarction remain uncertain.

The primary objective of this study was to determine the incidence of ischemia detected by ambulatory ECG monitoring in survivors of acute myocardial infarction and the prognostic value of this information considered independently of the results of exercise testing and the left ventricular ejection fraction. The secondary objective was to determine the prognostic value of all three

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types of information over and above that of routine clinical information.

## METHODS

### Enrollment of Patients

Consecutive patients were screened for eligibility at three coronary care units in Hamilton, Ontario, Canada. Each unit admits approximately 600 patients per year with acute myocardial infarction. The study was approved by the institutional review board at each participating hospital.

Patients with acute myocardial infarction who had survived for at least five days were eligible for enrollment. Myocardial infarction was defined as the presence of at least two of the following: characteristic ischemic pain lasting at least 20 minutes, an elevation of the creatine kinase or aspartate aminotransferase concentration to at least twice the upper limit of the normal range in the absence of another explanation or a creatine kinase MB value greater than 5 percent of the total creatine kinase concentration, and the development of new 40-msec Q waves in at least two adjacent ECG leads or the development of a dominant R wave in lead V<sub>1</sub>. (In the absence of pain and Q or R changes, the diagnosis of myocardial infarction could be made on the basis of an elevation of the creatine kinase concentration to a value at least twice the upper limit of the normal range, with no other explanation, plus a creatine kinase MB value greater than 5 percent of the total creatine kinase concentration.)

The criteria for exclusion from the study were ECG evidence at rest of left bundle-branch block, a diagnosis of the Wolff-Parkinson-White syndrome, left ventricular hypertrophy with a pattern of strain, or the presence of a permanent pacemaker; Canadian Cardiovascular Society class IV angina; New York Heart Association class IV heart failure; myocardial infarction as a complication of coronary angioplasty; and geographic, social, or other factors making participation impractical.

### Postinfarction Assessments

Patients underwent 48-hour ambulatory ECG monitoring between 5 and 7 days after the infarction, with submaximal exercise testing before discharge and an assessment of left ventricular function (by radionuclide angiography, two-dimensional echocardiography, or left ventriculography after the administration of contrast material) within 28 days after the infarction. Patients and physicians were unaware of the results of ambulatory ECG monitoring unless ventricular tachycardia or a severe conduction disturbance was present, in which case only the arrhythmia was disclosed.

### Ambulatory ECG Monitoring

Ambulatory ECG monitoring was performed with the use of two positive electrodes (leads V<sub>5</sub> and II) and AM cassette recorders with low and high cutoff frequencies of 0.05 and 100 Hz, respectively, a digital time display, and an event marker. The ambulatory ECG monitor was integrated into a playback system with a tape head that had the frequencies noted above. The ST-segment analysis was performed with a semiautomated, interactive quantitative program, and the result was reviewed by two observers experienced in ST-segment analysis, with differences resolved by consensus.

An ST-segment abnormality indicating ischemia on ambulatory ECG monitoring was defined as an ST-segment depression at least 1 mm below the base-line ST position measured at 80 msec beyond the J point, persisting for at least one minute and separated from a preceding episode by at least one minute. The number of episodes, cumulative duration of all episodes, maximal depression, and duration of the longest episode were recorded for each channel. To allow for variation in the total duration of monitoring, the number of episodes and total duration of the ST-segment depression were prorated for a 24-hour period. The channel with the maximal frequency of episodes was used for purposes of the analysis.

### Exercise Testing

Exercise testing was performed with the use of standard protocols for treadmill or bicycle ergometry. Twelve-lead ECG tracings were recorded by computer with the patient at rest, each minute during exercise, at peak exercise, and after exercise. The following data were recorded: workload achieved, in metabolic equivalents (MET); heart

rate and blood pressure at rest and during peak exercise; the amount of ST-segment depression 80 msec beyond the J point at rest and during peak exercise in three groups of leads (I and aVL; II, III, and aVF; and V<sub>1</sub> through V<sub>6</sub>); a qualitative assessment of the ST-segment slope; the occurrence of angina or its equivalent during exercise; and the primary reason for termination. The exercise test was terminated in the absence of symptoms if the heart rate reached 70 percent of the predicted maximal value or there was oxygen consumption of 5 MET, if the ST-segment depression was at least 1 mm below that recorded at rest in any one lead, or if there was a hypotensive response to exercise (a fall in systolic blood pressure by more than 20 mm Hg from the resting base-line value). An exercise test was considered positive if there was at least 1 mm of ST-segment depression 80 msec beyond the J point.

### Outcomes

The end points of death, nonfatal myocardial infarction, and unstable angina were tabulated at six months and one year. The diagnostic criteria for nonfatal myocardial infarction were identical to those at enrollment. A diagnosis of unstable angina was assigned if a patient had an exacerbation of angina resulting in hospitalization. At each center, outcome events were documented by the research nurse on the basis of appropriate medical records and were reviewed by the principal investigator. Deaths that occurred out of the hospital were reviewed with the next of kin, the patient's physician, or the coroner or with the use of autopsy data. All tests were analyzed without knowledge of the outcomes, and outcomes were analyzed without knowledge of the test results.

The prespecified primary outcomes were death, nonfatal myocardial infarction, and admission to the hospital because of unstable angina, but analyses were also planned for death alone and for death and nonfatal myocardial infarction combined.

### Statistical Analysis

The prognostic importance of the various assessments was determined in terms of the cumulative risk of an event at one year. Since data on patients without an outcome event were censored at the 12-month follow-up visit, there was little advantage in using actuarial methods. This simplification allowed most of the important analyses to be summarized as frequency tables with associated P values for comparisons between event rates based on Fisher's exact test.<sup>25</sup> The Kaplan-Meier technique was used to analyze the timing of outcome events during follow-up.<sup>26</sup> The marginal prognostic contribution of clinical data and the three postinfarction assessments was determined with the use of multiple logistic regression.<sup>27</sup> The effect of each variable on the outcome at one year is expressed as an odds ratio. The analytic strategy was to include in the model all prognostically valuable clinical variables and then add the postinfarction assessments in the order of their contribution to the prediction of the risk at one year. The models included only a main-effect term for each potential prognostic factor; no cross-product terms representing interactions were included. All reported P values are two-tailed.

## RESULTS

Between February 12, 1990, and November 5, 1991, 952 patients met the inclusion criteria, of whom 461 were excluded according to the protocol (177 with predefined resting ECG abnormalities, 46 with Canadian Cardiovascular Society class IV angina, 16 with New York Heart Association class IV heart failure, 7 with myocardial infarction after coronary angioplasty, and 215 for other reasons making participation impractical). Informed consent was obtained from 455 (93 percent) of the 491 remaining eligible patients. Forty-nine of these 455 patients were excluded because of technical problems with ECG monitoring (in the case of 39 patients) or failure to perform ambulatory monitoring (in the case of 10), leaving a cohort of 406 patients.

Ambulatory ECG monitoring (mean duration, 42

hours) was initiated on hospital day 5 to 7 after myocardial infarction in 400 patients and after discharge from the hospital (maximal period after infarction, 25 days) in 6. Pre-discharge submaximal exercise testing could not be performed in 73 patients for a variety of reasons, including the physician's refusal because of individual factors, musculoskeletal limitation, and scheduling problems. The left ventricular ejection fraction was determined in 372 patients (by radio-nuclide angiography in 235, by two-dimensional echocardiography in 94, and by left ventriculography after the administration of contrast material in 43). Follow-up data were complete for 405 of the 406 patients at one year.

The base-line characteristics of the 406 patients are shown in Table 1. The 49 patients without ambulatory ECG data were slightly older and a higher percentage had anterior or lateral infarcts, but they were otherwise similar to the study cohort.

#### Univariate Analysis

The results of the noninvasive tests and their association with the outcome events are shown in Table 2. Ambulatory ECG evidence of ischemia was present in 23.4 percent of the patients. Of the 333 patients in whom exercise testing was performed, 103 (30.9 percent) had positive tests, and the ejection fraction was abnormal ( $\leq 50$  percent) in 148 (40 percent) of the 372 patients in whom it was determined.

The overall mortality rate at one year was 5.7 percent, the rate of death or nonfatal myocardial infarction was 12.8 percent, and the rate of death, nonfatal

Table 2. Prognostic Value of Postinfarction Assessments.\*

ASSESSMENT	PATIENTS ASSESSED	OUTCOME		
		DEATH	NONFATAL MI OR DEATH	UNSTABLE ANGINA, NONFATAL MI, OR DEATH
<i>no. of patients/total no. (%)</i>				
Ambulatory ECG monitoring				
No ischemia	311/406 (76.6)	12/311 (3.9)	30/311 (9.6)	59/311 (19.0)
Ischemia	95/406 (23.4)	11/95 (11.6)	22/95 (23.2)	42/95 (44.2)
P value		0.009	0.001	<0.001
Exercise test				
Negative	230/333 (69.1)	7/230 (3.0)	23/230 (10.0)	48/230 (20.9)
Positive	103/333 (30.9)	4/103 (3.9)	11/103 (10.7)	24/103 (23.3)
Not done	73	12/73 (16.4)	18/73 (24.7)	29/73 (39.7)
P value		<0.001	0.007	0.007
Ejection fraction				
>50%	224/372 (60.2)	8/224 (3.6)	21/224 (9.4)	47/224 (21.0)
35–50%	115/372 (30.9)	4/115 (3.5)	17/115 (14.8)	30/115 (26.1)
<35%	33/372 (8.9)	6/33 (18.2)	9/33 (27.3)	14/33 (42.4)
Not determined	34	5/34 (14.7)	5/34 (14.7)	10/34 (29.4)
P value		0.001	0.03	0.06

\*P values were determined by global tests of differences in rates among assessment subcategories. MI denotes myocardial infarction.

myocardial infarction, or unstable angina requiring hospitalization was 24.9 percent. Table 2 shows the strong prognostic value of ambulatory ECG evidence of ischemia for each group of outcome events. The mortality rate at one year was 3.9 percent among the patients without ambulatory ECG evidence of ischemia and 11.6 percent among those with evidence of ischemia ( $P=0.009$ ; odds ratio for patients with ischemia, 3.3; 95 percent confidence interval, 1.3 to 8.4). Among the patients with ischemia, the odds ratio for death or nonfatal myocardial infarction was 2.8 ( $P=0.001$ ; 95 percent confidence interval, 1.5 to 5.4), and the odds ratio for death, nonfatal myocardial infarction, or unstable angina requiring hospitalization was 3.4 ( $P<0.001$ ; 95 percent confidence interval, 2.0 to 5.7). The prognostic value of ambulatory ECG evidence of ischemia in terms of the primary outcome events is shown in Figure 1.

The outcomes were similar among the patients with positive exercise tests and those with negative tests, but the rates for all outcomes were markedly higher among the patients in whom exercise testing was not performed (Table 2). The prognostic value of exercise testing was thus almost entirely dependent on whether testing was performed, rather than on the result. Alternative definitions of a positive exercise test, such as only a horizontal or down-sloping ST-segment depression or early termination of testing due to angina or hypotension, failed to enhance the predictive value of testing. Treatment with beta-blockers, calcium-channel blockers, or coronary angioplasty did not differ between the group of patients with positive exercise tests and the group with negative tests. The rate of coronary bypass surgery, however, was 18.4 percent in patients with positive tests but only 7.8 percent in those with negative tests ( $P=0.007$ ).

Table 2 shows only small differences in the risk of each outcome between the patients with a normal ejection fraction ( $>50$  percent) and those with an interme-

Table 1. Characteristics of 406 Patients with Acute Myocardial Infarction.\*

CHARACTERISTIC	VALUE
Age	
Mean (yr)	61.5 $\pm$ 11.8
$\geq 65$ yr (% of patients)	41.1
Male sex (% of patients)	77.8
Current smoker (% of patients)	39.9
History (% of patients)	
Angina	36.9
Myocardial infarction	19.8
Hypertension	34.1
Diabetes	15.3
Peak creatine kinase (U/liter)	1769 $\pm$ 1874
Q-wave infarction (% of patients)	59.5
Anterior or lateral infarction (% of patients)	41.2
Thrombolytic therapy (% of patients)	55.0
Postinfarction clinical findings (% of patients)	
Pulmonary edema	9.1
Angina	23.2
Congestive heart failure $\dagger$	2.7

\*Plus-minus values are means  $\pm$ SD.

$\dagger$ Defined as a requirement for ongoing therapy with digoxin or diuretics beyond day 7 after infarction.

diate ejection fraction (35 to 50 percent), but a clear elevation in risk among those with a low ejection fraction (<35 percent), particularly for mortality. The patients in whom the ejection fraction was not determined also had a somewhat higher risk of death, partly because some patients died before the ejection fraction could be determined.

There was no marked association between the number of episodes of ischemia during ambulatory ECG monitoring, the total duration of ischemia (per 24 hours), or the maximal length of an episode and any group of outcomes. The maximal ST-segment depression (1.0 to 2.4 mm vs.  $\geq 2.5$  mm) was associated with a somewhat elevated risk of each outcome, but with relatively few patients in each category, the difference in risk was not statistically significant.

#### Additional Prognostic Value of Ambulatory ECG Monitoring

Table 3 shows the additional prognostic value of ambulatory ECG monitoring, beyond the information provided by exercise testing. In each subgroup of patients (those with negative tests, those with positive tests, and those in whom testing was not performed) there is evidence of an association between the risk of an outcome event and the presence or absence of ischemia detected by ambulatory ECG monitoring. A logistic model fitted for each outcome included terms representing the result of the exercise test, the result of ambulatory ECG monitoring, and their interaction. The P values for the interaction terms were not significant for any outcome, indicating that these two tests provided independent prognostic information. With the interaction term omitted, the marginal prognostic contribution of ambulatory ECG monitoring was significant for each outcome. With the exception of mortality, the ambulatory ECG findings provided a statistically stronger contribution than the exercise test. In the analysis of death as the outcome, the P value was smaller when the exercise test was considered first, but the significance of this association was due to the "not done" category rather than to the test result itself.

Ambulatory ECG monitoring also yielded additional

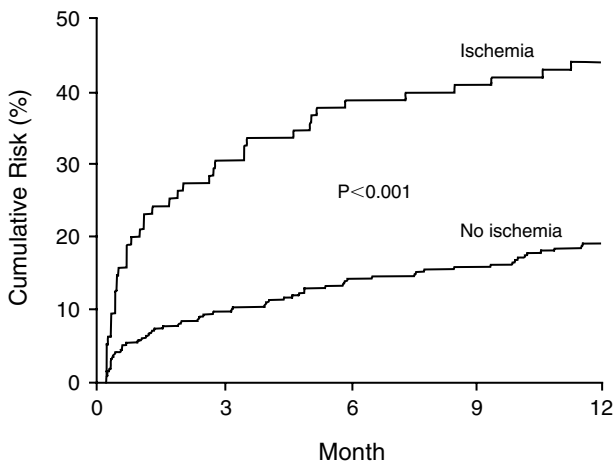


Figure 1. Cumulative Risk of Death, Nonfatal Myocardial Infarction, or Hospitalization for Unstable Angina, According to the Presence or Absence of Ischemia on Ambulatory ECG Monitoring in 406 Patients with Acute Myocardial Infarction.

Table 3. Joint Prognostic Value of Ambulatory ECG Monitoring and Exercise Testing.\*

ASSESSMENT	OUTCOME		
	DEATH	NONFATAL MI OR DEATH	UNSTABLE ANGINA, NONFATAL MI, OR DEATH
	no. of patients/total no. (%)		
Negative exercise test			
No ischemia	6/195 (3.1)	17/195 (8.7)	37/195 (19.0)
Ischemia	1/35 (2.9)	6/35 (17.1)	11/35 (31.4)
Positive exercise test			
No ischemia	2/68 (2.9)	6/68 (8.8)	8/68 (11.8)
Ischemia	2/35 (5.7)	5/35 (14.3)	16/35 (45.7)
Exercise test not done			
No ischemia	4/48 (8.3)	7/48 (14.6)	14/48 (29.2)
Ischemia	8/25 (32.0)	11/25 (44.0)	15/25 (60.0)
P value			
ECG monitoring, given exercise testing	0.037	0.003	<0.001
Exercise testing, given ECG monitoring	0.002	0.020	0.029
Interaction	0.38	0.47	0.20

\*MI denotes myocardial infarction.

independent prognostic information within subgroups of patients defined on the basis of the ejection fraction (Table 4). Although the ejection fraction was the stronger predictor of mortality, ischemia on ambulatory ECG monitoring represented additional prognostic information for the other outcome events.

Finally, we determined the sequence of various postinfarction assessments for the best prediction of the outcome (Table 5). In the first phase of modeling, the clinical variables listed in Table 1 were considered for stepwise selection. These clinical variables are readily available as a result of routine care; to justify the additional postinfarction assessments, they must be shown to have prognostic value over and above that of the clinical data. Once all the reasonably important clinical variables had been included in the model, the results of the postinfarction assessments were added in the order of their prognostic importance.

For the outcome of death, no postinfarction assessment provided prognostic information beyond that provided by the clinical variables. The odds ratio for a left ventricular ejection fraction of less than 35 percent, as compared with a higher value, was 2.5, which was not statistically significant. For the outcome of death or nonfatal myocardial infarction, the odds ratio for ambulatory ECG evidence of ischemia, as compared with its absence, was 2.3 ( $P = 0.009$ ); once this variable had been incorporated into the model, the other two variables (ejection fraction and exercise-test result) did not contribute significantly to the prognosis. The results were similar for the composite outcome of death, nonfatal myocardial infarction, and unstable angina.

#### DISCUSSION

The assessment of the risk of cardiac events after acute myocardial infarction has traditionally been based on the results of submaximal exercise testing before discharge and an evaluation of left ventricular function. This prospective study of a large cohort of patients surviving for at least five days after acute myocardial in-

**Table 4. Joint Prognostic Value of Ambulatory ECG Monitoring and Measurement of the Left Ventricular Ejection Fraction.\***

ASSESSMENT	OUTCOME		
	DEATH	NONFATAL MI OR DEATH	
		UNSTABLE ANGINA, NONFATAL MI, OR DEATH	
<i>no. of patients/total no. (%)</i>			
Ejection fraction >50%			
No ischemia	6/178 (3.4)	12/178 (6.7)	31/178 (17.4)
Ischemia	2/46 (4.3)	9/46 (19.6)	16/46 (34.8)
Ejection fraction 35–50%			
No ischemia	1/91 (1.1)	11/91 (12.1)	18/91 (19.8)
Ischemia	3/24 (12.5)	6/24 (25.0)	12/24 (50.0)
Ejection fraction <35%			
No ischemia	3/20 (15.0)	5/20 (25.0)	6/20 (30.0)
Ischemia	3/13 (23.1)	4/13 (30.8)	8/13 (61.5)
Ejection fraction not measured			
No ischemia	2/22 (9.1)	2/22 (9.1)	4/22 (18.2)
Ischemia	3/12 (25.0)	3/12 (25.0)	6/12 (50.0)
P value			
ECG monitoring, given ejection fraction	0.034	0.002	<0.001
Ejection fraction, given ECG monitoring	0.010	0.083	0.13
Interaction	0.40	0.83	0.59

\*MI denotes myocardial infarction.

fraction demonstrates that myocardial ischemia detected by ambulatory ECG monitoring is common early after infarction and that its presence is an important predictor of the outcome during the subsequent year.

The incidence of ischemia detected by ambulatory ECG monitoring in this study was 23 percent. The reported incidence of ambulatory ECG ischemia after acute myocardial infarction ranges from 8 to 46 percent.<sup>14-24</sup> In these studies ambulatory ECG monitoring was performed as early as 3 days<sup>16</sup> or as late as 20 years<sup>14</sup> after acute myocardial infarction. These studies also varied with regard to the characteristics of the enrolled patients (unstable angina,<sup>20</sup> only a first myocardial infarction,<sup>17,22,24</sup> left ventricular dysfunction and

ventricular arrhythmias,<sup>15</sup> or eligibility for participation in a thrombolytic trial<sup>18</sup>). Our study reports the prevalence of ischemia on ambulatory ECG monitoring in consecutive patients early after Q-wave or non-Q-wave infarction and irrespective of the administration of thrombolytic agents or a history of infarction, and with a commonly accepted definition of ST-segment depression.

Our results are consistent with those of prior studies showing that the ST-segment depression on exercise testing has a low predictive accuracy.<sup>3-6</sup> In our study, however, physicians were not blinded to the results of exercise testing, and its lack of prognostic value may have been due to a higher rate of bypass surgery in the subgroup of patients with positive exercise tests. It is also possible that the mechanism underlying the development of an ST-segment depression on ambulatory ECG monitoring differs from that of ischemia detected during exercise testing and carries a more ominous prognosis.

The logistic-regression analysis was performed in an attempt to answer the following question: Given the standard clinical information available after acute myocardial infarction, what additional prognostic information is provided by ambulatory ECG monitoring, exercise testing, or measurement of the ejection fraction? None of these assessments contributed significantly to the prediction of the risk of death, perhaps because of the small numbers of deaths and the strong predictive value of the presence or absence of postinfarction congestive heart failure. The Multicenter Postinfarction Research Group previously reported the independent contribution of the left ventricular ejection fraction to the prediction of mortality, but the clinical assessment of heart failure at the time of infarction also made a significant contribution.<sup>28</sup> When the ischemic events of nonfatal myocardial infarction and hospitalization because of unstable angina were considered as outcome

**Table 5. Marginal Prognostic Value of Postinfarction Assessments.\***

ORDER OF ENTRY INTO MODEL	DEATH			NONFATAL MI OR DEATH			UNSTABLE ANGINA, NONFATAL MI, OR DEATH		
	VARIABLE	OR (95% CI)	P VALUE	VARIABLE	OR (95% CI)	P VALUE	VARIABLE	OR (95% CI)	P VALUE
<b>Clinical variables</b>	Post-MI CHF	10.4 (2.5–44.5)	0.010	Anterior MI	2.6 (1.4–4.8)	0.002	Anterior MI	2.1 (1.3–3.3)	0.003
	Male sex	0.3 (0.1–0.7)	0.031	History of diabetes	2.8 (1.4–5.8)	0.003	Post-MI angina	2.0 (1.2–3.4)	0.010
	Age ≥65 yr	3.9 (1.2–12.6)	0.065	Male sex	0.4 (0.2–0.9)	0.014	Male sex	0.5 (0.3–0.9)	0.031
	Smoker	0.3 (0.1–1.2)	0.156	Age ≥65 yr	1.8 (1.0–3.5)	0.050	History of diabetes	1.8 (1.0–3.4)	0.055
	History of hypertension	2.1 (0.8–5.3)	0.219	Post-MI CHF	3.1 (0.8–11.3)	0.082	Age ≥65 yr	1.5 (0.9–2.4)	0.106
	History of diabetes	2.2 (0.8–6.2)	0.230	Post-MI angina	1.8 (0.8–3.1)	0.201	Prior MI	1.6 (0.9–2.9)	0.106
							Post-MI CHF	2.8 (0.7–10.5)	0.130
<b>First additional assessment</b>	EF >50%	1.0	0.162	Ischemia	2.3 (1.2–4.5)	0.009	Q-wave MI	1.5 (0.9–2.4)	0.131
	EF 35–50%	0.8 (0.2–3.3)			Ischemia		2.8 (1.6–4.8)	<0.001	
	EF <35%	2.5 (0.6–10.4)							
	Not done	4.4 (1.2–16.2)							
<b>Second additional assessment</b>	Ischemia	2.2 (0.8–6.0)	0.276	Exercise –	1.0	0.270	Exercise –	1.0	0.492
				Exercise +	0.8 (0.4–1.9)		Exercise +	0.9 (0.5–1.7)	
				Not done	1.3 (0.8–3.6)		Not done	1.4 (0.7–2.6)	
<b>Third additional assessment</b>	Exercise –	1.0	0.439	EF >50%	1.0	0.475	EF >50%	1.0	0.520
	Exercise +	0.9 (0.2–3.5)		EF 35–50%	1.6 (0.7–3.3)		EF 35–50%	1.3 (0.7–2.4)	
	Not done	2.6 (0.8–8.1)		EF <35%	2.0 (0.7–5.6)		EF <35%	1.7 (0.7–4.3)	
				Not done	1.1 (0.4–3.4)		Not done	1.1 (0.4–2.6)	

\*Variables are listed in the order of their entry into the model. MI denotes myocardial infarction, OR odds ratio, CI confidence interval, CHF congestive heart failure, EF left ventricular ejection fraction, “Exercise –” a negative exercise test, and “Exercise +” a positive exercise test. Unless otherwise noted, the reference category for the odds ratio for each variable is the absence of that variable.

events in our study, ambulatory ECG evidence of an ST-segment depression was the only test variable that provided incremental prognostic information beyond that provided by the clinical variables, with the detection of ischemia more than doubling the risk of an outcome event.

Ambulatory ECG evidence of an ST-segment depression had a low predictive value for death alone (12 percent) but when nonfatal myocardial infarction and unstable angina were included as outcomes, the predictive value improved (44 percent). Ambulatory ECG monitoring provided prognostic information for patients in whom exercise testing was not performed and for those with positive or negative exercise results, as well as for patients with an abnormal or normal left ventricular ejection fraction. It would therefore be logical to use ambulatory ECG monitoring as the screening test of choice after acute myocardial infarction and to reserve submaximal exercise testing and measurement of the left ventricular ejection fraction for selected cases in which specific information is needed.

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