Prognostic Value of a Normal or Nonspecific Initial Electrocardiogram in Acute Myocardial Infarction

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Context Although previous studies have suggested that normal and nonspecific initial electrocardiograms (ECGs) are associated with a favorable prognosis for patients with acute myocardial infarction (AMI), their independent predictive value for mortality has not been examined.

Objective To compare in-hospital mortality among patients with AMI who have normal or nonspecific initial ECGs with that of patients who have diagnostic ECGs.

Design, Setting, and Patients Multihospital observational study in which 391 208 patients with AMI met the study criteria between June 1994 and June 2000 and had ECGs that were normal (n=30 759), nonspecific (n=137 574), or diagnostic (n=222 875; defined as ST-segment elevation or depression and/or left bundle-branch block). A logistic regression model was constructed using a propensity score for ECG findings and data on demographics, medical history, diagnostic procedures, and therapy to determine the independent prognostic value of a normal or nonspecific initial ECG.

Main Outcome Measures In-hospital mortality; composite outcome of in-hospital death and life-threatening adverse events.

Results In-hospital mortality rates were 5.7%, 8.7%, and 11.5% while the rates of the composite of mortality and life-threatening adverse events were 19.2%, 27.5%, and 34.9% for the normal, nonspecific, and diagnostic ECG groups, respectively. After adjusting for other predictor variables, the odds of mortality for the normal ECG group was 0.59 (95% confidence interval [CI], 0.56-0.63; $P<.001$) and for the nonspecific group was 0.70 (95% CI, 0.68-0.72; $P<.001$), compared with the diagnostic ECG group.

Conclusion In this large cohort of patients with AMI, patients presenting with normal or nonspecific ECGs did have lower in-hospital mortality rates than those of patients with diagnostic ECGs, yet the absolute rates were still unexpectedly high.

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Studies of patients presenting to the emergency department with chest pain have found that a normal or nonspecific electrocardiogram (ECG) portends a low rate of mortality and life-threatening complications.[1-8] Deferred outpatient testing (within 72 hours) is therefore frequently recommended for these low-risk patients.[8,9] These studies were often carried out at single hospitals,[1-4,6-8] and some have combined patients who have nonspecific ECG findings with those who have normal ECG results.[1,8] Most importantly, they all contained only a small subgroup of patients with objectively confirmed acute myocardial infarction (AMI) who have normal initial ECGs.

The mortality rate of patients with proven AMI and a normal initial ECG has not been well described and may be quite high.[5,7,10] A recent analysis by Pope et al[10] found that 2.1% of patients with AMI were inadvertently discharged from the emergency department. A normal ECG finding was the most likely predictor of inadvertent discharge of these patients, and among patients sent home with AMI, the 30-day mortality rate was 10.5%.

To date, there has been no large multihospital study of patients with AMI that has addressed the independent prognostic value of a normal or nonspecific initial ECG. The National Reg-

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istry of Myocardial Infarction (NRMI)[11] affords an opportunity to compare the risk of in-hospital death and life-threatening complications among patients with normal and diagnostic initial ECGs. The main objective of this study was to determine the predictive value of the initial ECG for in-hospital mortality.

METHODS

Study Population and Data Collection

The NRMI is an observational database of hospitalized patients with confirmed AMI that was instituted in 1989. The NRMI 2 enrolled patients at 1674 hospitals from June 1994 through April 1998. This was followed by the NRMI 3, which included data from 1553 hospitals (through June 2000).[12] The data collection and results of this registry are comparable to the those of the Cooperative Cardiovascular Project (CCP), but the NRMI includes all payers as opposed to only Medicare beneficiaries.[13]

In the NRMI, the diagnosis of myocardial infarction was based on a clinical presentation consistent with AMI and at least 1 of the following findings: creatine kinase or creatine kinase-MB greater than or equal to twice the upper limit of normal, electrocardiographic evidence of AMI, elevation of other cardiac specific enzymes (NRMI 3), scintigraphic or autopsy evidence of myocardial infarction, or a discharge diagnosis of myocardial infarction by the *International Classification of Diseases, Ninth Revision, Clinical Modification* code 410.X1 (NRMI 2). For the NRMI 3, a discharge diagnosis of myocardial infarction was required. Data were abstracted from the medical record by a trained site study coordinator and were transcribed onto a case report form. The case report forms were sent to StatProbe, Inc, Lexington, Ky, and the data entered underwent multiple checks for accuracy. Any inconsistencies or unrecorded fields were returned to the site for clarification and correction. All ECG results coded in the NRMI database were abstracted from the final reading found on the medical record after patient discharge.

Patients who were eligible for inclusion in this study were those entered in the NRMI 2 (n=772 586) and the NRMI 3 database (n=537 444) through June 2000 (a total of 1 310 030 patients). We excluded from analysis all patients who were transferred to or from other facilities since we could not always ascertain the results of the initial ECG and outcome data were not always available (554 550 cases). Also excluded were patients who had the first ECG obtained for reasons other than symptoms of AMI (defined as chest pain or pressure, arm or jaw pain, dyspnea, nausea and vomiting, syncope, and/or cardiac arrest; 22 289 cases). The percentage of nontransferred patients diagnosed with AMI who at presentation had normal or nonspecific initial ECGs was determined.

We excluded patients found to have Killip class III or IV heart failure on initial presentation because these findings were part of the composite outcome measure (77 215 cases). An additional 264 768 patients were removed based on the following findings on the initial ECG: Q waves, right bundle-branch block, or multiple different readings of the initial ECG (such as ST-segment elevation and normal in the single ECG reading), or when the results of the initial ECG were not available. The final study population included 391 208 patients. For analysis, they were divided into 3 groups based on the initial ECG; normal, those with nonspecific ST-segment and/or T-wave changes, and diagnostic of AMI (defined as ST-segment elevation, ST-segment depression, and/or left bundle-branch block).

Variables and Outcomes Measures

Registry variables collected included demographics, previous history, presentation, treatment, procedures, complications, and in-hospital mortality. Times from symptom onset to hospital arrival as well as other clinically important time intervals were abstracted from the medical record. To prevent the influence of outliers, any patient with a value greater than 72 hours was assigned a time of 72 hours.

The main outcome measure was in-hospital mortality. A secondary outcome was the composite of in-hospital mortality and/or adverse in-hospital events (defined as ventricular tachycardia or fibrillation, the development of pulmonary edema or cardiogenic shock [Killip class III or class IV heart failure], and/or hypotension requiring intervention). No special weighting was given to each factor in the composite outcome.

Statistical Analysis

An analysis of baseline patient characteristics was conducted to compare the 3 groups. Differences between the groups were assessed by χ^2 tests for categorical variables. For continuous data, analysis of variance and Kruskal-Wallis were used. Mortality rates as a function of the findings on the initial ECG were compared by χ^2 tests. Stratified analyses were performed according to a number of prespecified clinical and demographic variables. To evaluate the impact of higher presenting grades of heart failure or ECG-related mortality differences, we reintroduced patients with Killip class III and IV heart failure.

To assess the independent prognostic valve of the initial ECG, we generated 2 propensity scores using logistic regression to predict the likelihood of having a normal or a nonspecific ECG vs a diagnostic ECG.[14] The *c* statistic was calculated to determine the ability of the model to discriminate between patients with and without diagnostic ECGs. Relevant variables were then used to construct a series of forward logistic regression models with in-hospital mortality as the dependent variable. The first model incorporated the propensity score to derive the adjusted odds for mortality with the initial ECG being the main independent variable. Subsequently, demographics (age, sex, race), followed by prior history (smoking, hypercholesterolemia, prior AMI, percutaneous coronary intervention [PCI], or coronary artery bypass graft surgery), presence of Killip class II heart failure on admission, infarct location, medications administered within 24 hours (aspirin, nitroglycerin, β-blockers, lidocaine, angiotensin-converting enzyme inhibitors, calcium channel blockers, and antiplatelet therapies), diagnostic procedures (heart catheterization, and echocardiographic assessment of cardiac function), and finally reperfusion therapies (PCI or intravenous thrombolytics) were added to the model in successive blocks.

To further evaluate our findings, the propensity scores were used to generate 2 subsets of closely matched subjects to compare first, the normal ECG group, and then the nonspecific ECG group with the diagnostic ECG group.[14] For these matched samples, the signed rank test was used to compare continuous data and the McNemar test was used for binary data.

The reported *P* values are all 2-tailed. It must be noted that, due to the extremely large number of patients, care must be exercised when interpreting the clinical importance of all *P* values. All statistical analyses were perfromed using SAS software 8.02 (SAS Institute, Cary, NC).

RESULTS

Among all 733 191 nontransfer patients with AMI, 4.4% (32 172) had a normal, 20.8% (152 659) had a nonspecific, and 33.6% (246 440) had a diagnostic initial ECG. After application of other exclusion criteria, 391 208 were eligible for analysis. The mean age was 67.8 years (25th percentile, 51.7 years; 75th percentile, 79.0 years; range, 18-107 years). Whites accounted for 84.4% of the study population, and 59.0% of the study patients were men. Medicare was the largest payer group (44.1%), followed by commercial or preferred provider organizations (27.4%), health maintenance organizations (13.6%), and Medicaid (2.9%).

Of the patients eligible for this study, 7.9% had normal, 35.1% had nonspecific, and 57.0% had diagnostic initial ECGs. Patients with a normal initial ECG tended to be younger, male, and had lower rates of prior myocardial infarction and congestive heart failure (CHF) whereas patients with nonspecific ECGs had the highest rate of prior angina, myocardial infarction, and CHF. Conversely, patients with a normal initial ECG had higher rates of previous PCI and hypercholesterolemia (**TABLE 1**).

There were differences between the groups noted at the time of hospitalization (**TABLE 2**). Fewer patients with normal or nonspecific ECGs arrived at the hospital within 6 hours of the onset of symptoms. These same 2 groups were noted to have less typical symp-

Table 1. Baseline and Facility Characteristics*

Characteristics	Electrocardiogram Results: Normal (n = 30 759)	Nonspecific (n = 137 574)	Diagnostic (n = 222 875)	*P* Value
Age, mean (SD), y	65.2 (14.5)	69.6 (13.8)	67.2 (14.3)	<.001
<65	48.2	34.9	42.4	<.001
65-75	22.9	25.4	24.3	<.001
≥75	28.8	39.7	33.2	<.001
Sex				
Women	37.7	44.2	39.5	<.001
Men	62.3	55.8	60.5	<.001
Race				
White	84.0	83.5	85.0	<.001
Black	7.4	9.0	6.7	<.001
Hispanic	3.4	2.9	3.1	<.001
American Indian or Alaskan	0.2	0.2	0.2	.73
Asian or Pacific Islander	1.6	1.5	1.5	.34
Other	3.4	2.9	3.5	<.001
Medical history				
Myocardial infarction	21.0	27.8	22.1	<.001
Angina	14.8	17.3	13.8	<.001
Congestive heart failure	9.9	17.1	11.6	<.001
Percutaneous intervention	10.3	9.8	8.7	<.001
CABG surgery	10.8	15.4	10.4	<.001
Stroke	7.5	10.7	8.4	<.001
Diabetes	23.7	30.6	24.4	<.001
Hypertension	50.9	56.9	50.7	<.001
Hypercholesterolemia	30.8	27.0	27.1	<.001
Smoker	26.4	21.5	28.9	<.001
Family history of CAD	29.6	25.0	27.3	<.001
Payer status				
Commercial or PPO	32.3	25.3	28.0	<.001
HMO	16.8	13.1	13.4	<.001
Medicare	36.6	48.5	42.4	<.001
Medicaid	2.9	3.1	2.7	<.001
Veteran Affairs or CHAMPUS	0.5	0.5	0.5	.07
Self-pay or uninsured	4.9	3.8	5.8	<.001
Other	6.0	5.7	7.0	<.001
Hospital myocardial infarction volume, quartile				
First	3.9	4.2	4.7	<.001
Second	11.5	12.1	12.5	<.001
Third	24.5	24.3	24.4	.51
Fourth	60.1	59.4	58.4	<.001

*Data are presented as percentages unless otherwise indicated. CABG indicates coronary artery bypass graft surgery; CAD, coronary artery disease; PPO, preferred provider organization; HMO, health maintenance organization; and CHAMPUS, Civilian Health and Medical Program of the Uniformed Services.

toms of myocardial infarction, less often given an admitting diagnosis of myocardial infarction, less frequently admitted to an intensive care unit, but more often admitted to a monitored bed. Median times from hospital arrival to obtaining the first ECG were longer for patients with normal ECGs and nonspecific ECGs.

Hospitalization characteristics according to the baseline ECG are summarized in TABLE 3. Patients with normal or nonspecific ECGs had a much higher prevalence of non–Q-wave infarctions. Those with normal ECGs were found to have higher mean (SD) ejection fractions: normal, 53% (14%); nonspecific, 48% (15%); and diagnostic 47% (14%) ECGs; $P<.001$. Those with normal or nonspecific ECGs were less often treated with aspirin, heparin, intravenous β-blockers, or PCI but had similar rates of coronary artery bypass graft surgery.

In-Hospital Mortality and Life-Threatening Complications

The overall in-hospital mortality rates for the final study population were 5.7% with normal, 8.7% with nonspecific, and 11.5% with diagnostic initial ECGs and the composites of death and serious cardiac event rates were 19.2%, 27.5%, and 34.9%, respectively. Compared with patients with a diagnostic ECG, the unadjusted OR for death for patients with normal ECGs was 0.47 (95% CI, 0.44-0.49; $P<.001$) and for nonspecific ECGs, 0.74 (95% CI, 0.72-0.75; $P<.001$) compared with those with diagnostic ECGs. When death occurred it was earlier in the hospital course among patients with diagnostic ECGs (mean, 2.5 days; interquartile range, 0.7-6.0 days) than for patients with normal (mean, 4.3 days; interquartile range, 1.9-9.5 days) or nonspecific (mean, 4.3 days; interquartile range, 1.7-8.9 days, $P<.001$) ECGs. The FIGURE shows the survival distribution for patients remaining hospitalized at the given times.

Among patients with normal or nonspecific initial ECGs, 20.1% and 18.4%, respectively, developed frank ST-segment elevation or left bundle-branch block on subsequent ECGs, and these patients had mortality rates of 9.2% and 12.3%, respectively. For patients with normal initial ECGs, those having a prior history of cardiac disease had a 5.8% mortality rate, which was not significantly different from patients without a history of cardiac disease (5.7%, $P=.70$) and (although statistically significant) clinically this was true for the patients with nonspecific ECGs (8.4% vs 8.9%, $P<.001$). However, among patients with diagnostic ECGs, the mortality for those with prior cardiac disease was slightly higher (12.5% vs 11.1%, $P<.001$) than for those without prior cardiac disease.

The addition of patients presenting with Killip class III or class IV heart failure had only minimal effect on in-hospital mortality for the normal ECG group, a small effect on those with nonspecific ECGs but a more pronounced effect on patients with diagnostic ECGs (normal, 6.2%; nonspecific, 9.8%; and diagnostic, 13.6%). This is, in part, due to the relatively small fraction of patients with normal initial ECGs who present with higher Killip classes of heart failure (4.5%) vs patients with nonspecific (9.9%) or diagnostic initial ECGs (9.6%).

When examining the mortality among subgroups of patients with certain clinical characteristics in the various ECG groups, it was noted that the lack of chest pain as a presenting symptom, age greater than 75 years, tachycardia, and Killip class II heart failure on presentation were

Table 2. Clinical Findings at Hospital Presentation, Initial Diagnosis, and Admission Site*

Characteristics	Electrocardiogram (ECG): Normal (n = 30 759)	Nonspecific (n = 137 574)	Diagnostic (n = 222 875)
Time of symptom onset to ED presentation, min†			
<360	47.4	44.4	63.8
≥360	18.6	20.0	15.4
Data missing	33.9	35.6	20.7
Chest pain as presenting symptom‡	64.8	61.7	78.7
Blood pressure, mean (SD), mm Hg			
Systolic	149 (30)	148 (32)	141 (33)
Diastolic	83 (18)	81 (19)	80 (20)
Pulse, mean (SD), beats/min	83 (19)	87 (22)	83 (23)
Time of hospital arrival to first ECG, median (25th, 75th percentile), min	15 (7, 35)	15 (7, 36)	10 (5, 21)
Killip class (assessment of heart failure on presentation)			
I (none)	88.7	78.4	82.3
II (rales/JVD)	11.3	21.6	17.7
Admission diagnosis			
Myocardial infarction	15.3	16.7	66.0
Rule out myocardial infarction	36.9	37.2	15.7
Unstable angina	20.6	18.5	7.2
Other	27.2	27.6	11.1
Admission location§			
Intensive care unit or cardiac care unit	49.2	55.0	84.5
Monitored bed	44.9	40.4	13.6
Unmonitored bed	5.9	4.6	1.9

*Because of the large number of patients, care must be used when interpreting the clinical significance of the P values, all of which are <.001. Data are presented as percentages unless otherwise indicated. ED indicates emergency department; JVD, jugular venous distention.
†Symptoms are those of myocardial infarction and include chest pain or pressure, arm or jaw pain, dyspnea, nausea or vomiting, syncope, and/or cardiac arrest. Other than chest pain, these specific symptoms were not abstracted from the medical record.
‡Chest pain includes chest discomfort, pressure, arm, or jaw pain. It does not include dyspnea, nausea or vomiting, or other gastrointestinal symptoms, palpitations, syncope, or cardiac arrest.
§Admission location was only available for patients in the National Registry for Myocardial Infarction 2 registry (n = 230 529). There were 4956 missing values, leaving 225 573 patients with available data.

among the factors associated with increased mortality rates. However, for patients who were younger than 65 years (particularly men) or had ejection fractions of 40% or higher, a normal ECG predicted a low in-hospital mortality rate (TABLE 4).

Logistic Regression Model and Matched Pairs Analysis

After adjusting for propensity score and all variables in our model, a normal initial ECG remained a strong predictor of a lower mortality rate (adjusted OR, 0.59; 95% CI, 0.56-0.63; $P<.001$) as was a nonspecific ECG (OR, 0.70; 95% CI, 0.68-0.72; $P<.001$) (TABLE 5). The *c* statistics for the propensity score derivations were 0.82 and 0.78, and the *c* statistics for the final model were 0.85 for the normal and 0.83 for the nonspecific ECG groups.

After propensity score matching, the many baseline differences between groups largely disappeared (TABLE 6). The matched normal and diagnostic ECG groups were found to have in-hospital mortality rates of 5.7% and 9.5%, respectively (OR, 0.58; 95% CI, 0.54-0.61; $P<.001$). For the matched nonspecific and diagnostic ECG groups, the respective mortality rates were 8.7% and 12.5% (OR, 0.67; 95% CI 0.65-0.69; $P<.001$).

Table 3. Infarct Characteristics and Treatments During Hospitalization*

Characteristics	Electrocardiogram (ECG): Normal (n = 30 759)	Nonspecific (n = 137 574)	Diagnostic (n = 222 875)
Infarct location†			
Anterior or septal	13.2	15.9	30.4
Inferior	16.9	17.5	45.0
Posterior	3.2	3.0	6.3
Lateral	7.7	9.5	16.7
Right ventricle involved	0.2	0.2	1.1
Not specified	65.7	62.1	20.9
Type of myocardial infarction			
Non–Q wave	82.0	81.6	41.0
Q wave	18.0	18.4	59.0
Ejection fraction, %‡			
<40	13.5	23.8	25.8
≥40	86.5	76.2	74.2
Therapy			
Aspirin within 24 h	81.0	77.9	84.8
Heparin	64.9	64.0	81.7
Intravenous nitroglycerin	42.7	44.4	67.2
Oral β-blocker	44.5	41.4	41.4
Intravenous β-blocker	9.5	9.3	21.8
ACE inhibitor	16.6	21.2	18.3
Calcium channel blocker	17.2	20.0	11.5
Thrombolytic therapy	4.2	3.3	33.5
PCI	24.9	19.3	33.8
CABG surgery	9.6	9.4	9.8
Glycoprotein IIb/IIIa inhibitor§	12.2	10.3	22.8

*Data are presented as percentages unless otherwise indicated. All *P* values are <.001. ACE indicates angiotensin-converting enzyme; PCI, percutaneous coronary intervention; and CABG, coronary artery bypass graft.
†The percentages add up to more than 100% because some patients had multiple infarct locations.
‡The percentage is that of patients with data available for ejection fraction. Of the total patient population, 41.0% of those with normal, 39% of those with nonspecific, and 37.9% of those with diagnostic ECGs had missing ejection fraction data ($P<.001$).
§National Registry of Myocardial Infarction 3 only.

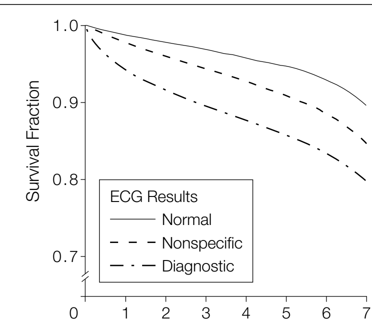
COMMENT

Our study has shown that for patients with AMI, those with normal or nonspecific initial ECGs had lower but clinically significant short-term mortality rates compared with those with diagnostic ECGs. Analysis of variables possibly predictive of the outcome had a small impact on the adjusted OR. For patients with AMI, a normal initial ECG was associated with a 41% lower risk of in-hospital death.

The unexpected finding of this study was that patients with an initially normal ECG had a substantial mortality rate, one that approximates the 30-day risk for patients with ST-segment elevation treated in recent trials of reperfusion therapies. Patients with nonspecific ECGs had a mortality rate in excess of those in the same clinical trials.[15-18] Our results demonstrate that, for patients with AMI, a normal or nonspecific initial ECG does not always indicate that the patient will have a favorable hospital course. This is underscored by the rate of combined mortality and potentially life-threatening adverse events (normal, 19.2%; nonspecific, 27.5%) experienced by these groups. Our findings are in contrast to other smaller studies of patients with a normal or nonspecific initial ECG.[1-8] Of particular interest is our identification of 2 subgroups of patients with a normal ECG who did have a very low mortality (Table 4): men younger than 65 years and those patients with an ejection fraction of 40% or greater.

Prior studies have determined that a normal or nonspecific initial ECG in the

Figure. Survival Distribution Based on Electrocardiogram (ECG) Findings



No. at Risk	0	2	4	7
Normal	30 759	24 383	14 236	8013
Nonspecific	137 574	116 388	76 596	46 209
Diagnostic	222 875	187 842	122 873	70 377

The survival distribution function curves represent the unadjusted fraction of survivors as a function of remaining hospitalized patients at the given time (patients at risk).

setting of possible acute cardiac ischemia carries a favorable prognosis[1-8] and minor ECG changes are predictive of a good outcome among patients with unstable coronary syndromes.[19,20] In contrast, Zalenski et al[21] found that for patients with AMI who have a benign initial ECG, those who later develop diagnostic ECGs are more prone to in-hospital life-threatening complications. Our study confirmed this and showed the mortality rate for patients with a normal initial ECG who later develop ST-segment elevation or left bundle-branch block was 9.2% and among patients with initial nonspecific ECGs who developed the same findings, the mortality rate was higher (12.3%) than that of patients who presented with diagnostic ECGs. Thus, abnormalities found on subsequent ECGs help define the patient's risk of death.

It is worthwhile exploring why the mortality rate of our cohort of patients with normal initial ECGs is similar to that of patients with diagnostic ECGs treated in clinical trials. The NRMI study population is drawn from a broad spectrum of hospitals and therefore may be more representative of patients with AMI. Clinical trials are commonly performed at higher-volume institutions that have more experience treating AMI and perform more cardiac procedures (factors associated with lower mortality rates).[22-24] Many of our patients may have had comorbid illness or informed consent issues that would have excluded them from clinical trials. There were delays in seeking medical care among patients with normal initial ECGs that can negatively influence outcome.[15,25,26] Patients with normal or nonspecific ECGs presented with chest pain less frequently than did patients with diagnostic ECGs. A recent study has shown that patients with AMI but had no chest pain delay seeking medical care, receive less aggressive care, and have significantly increased mortality rates.[27] Patients with AMI who present with a normal ECG were less often treated with aspirin, heparin, and β-blockers. Finally, a strategy of very early catheterization and PCI in patients with AMI and non–ST-segment elevation ECGs may be associated with better outcomes.[28,29] Our observations of the prognosis and the relative undertreatment of these patients indicate there may be significant opportunity for more aggressive therapy with the hope of improved outcomes.

Our results also have implications for the approximately 2% to 4% of patients with AMI who are inadvertently discharged from the emergency department.[10,30] The rate of inappropriate discharge has been shown to be 7.7 times more likely for patients with normal ini-

Table 4. Mortality Rates for Patients With the Specified Initial Electrocardiogram (ECG) Findings and the Given Characteristics

	ECG		
Characteristic	Normal	Nonspecific	Diagnostic
Total mortality	5.7	8.7	11.5
Sex			
Men by age, y			
<65	1.5	2.7	3.5
65-74	5.7	7.4	10.2
≥75	11.7	14.3	19.6
Women by age, y			
<65	3.0	4.9	6.3
65-74	7.3	8.7	13.3
≥75	11.5	13.7	21.7
Race			
White	5.8	8.9	11.7
Nonwhite	5.1	7.7	10.2
History of congestive heart failure	14.0	14.9	21.5
History of myocardial infarction	6.2	9.0	13.0
No chest pain on presentation	11.4	14.7	24.4
Clinical findings on hospital arrival			
Killip class heart failure			
I (none)	4.8	6.9	9.3
II (rales/JVD)	12.8	15.2	21.7
Heart rate, beats/min			
<100	4.8	7.3	9.3
≥100	10.5	12.9	18.5
Ejection fraction, %			
<40	11.9	12.4	15.6
≥40	2.3	3.8	4.0
Admission diagnosis			
Myocardial infarction	4.2	7.9	10.4
Rule out myocardial infarction	2.6	5.3	9.1
Unstable angina	2.6	4.2	6.6
Other	13.1	16.9	23.8

*The values are presented as percentages and are unadjusted mortality rates for patients in each of the 3 ECG groups.

Table 5. Odds Ratios (ORs) for Death for Patients With Normal and Nonspecific Electrocardiogram (ECG) Results*

	OR (95% CI)	
Model	Normal	Nonspecific
Unadjusted	0.47 (0.44-0.49)	0.74 (0.72-0.75)
Adjusted for the propensity score†	0.58 (0.55-0.61)	0.68 (0.66-0.70)
Adjusted for above and other variables‡	0.59 (0.56-0.63)	0.70 (0.68-0.72)

*Mortality of patients with an initial diagnostic ECG is the reference. CI indicates confidence interval. All *P* values are <.001.

†The propensity score is the probability of having a normal (or nonspecific) initial ECG, as opposed to a diagnostic ECG, based on a multivariable logistic regression model. See "Methods" section for details.

‡Other variables in the final model included demographics, presenting clinical data, medications administered within the first 24 hours, diagnostic procedures, and therapeutic interventions (the "Methods" section lists all included variables).

tial ECGs.[10] These patients sustain short-term mortality rates of 10.5% to 26%[5,10,30] and have a risk-adjusted mortality ratio of 1.9 times those of patients with AMI who are not discharged.[10] A strategy of using several biomarkers of myocardial necrosis may help identify these at-risk patients.[31]

Limitations of this study include that the ECG data abstracted from the medical record were not examined by a core laboratory. Electrocardiogram results were obtained from the final reading found on the chart after hospital discharge. These readings are most commonly physician edited computerized ECG readings. The computerized ECG reading of "normal" is highly reliable, identifying normal ECGs correctly in 99.4% to 100% of cases.[32,33] For patients with suspected AMI, a computer-interpreted ECG can effectively screen for thrombolytic candidates.[34] Computer assisted ECG readings improved the concordance of the physician's reading with the expert reading,[35] and it is very efficient and cost effective for large population-based research.[36] The inclusion of multiple different hospitals and ECG interpretation by computer and different physicians allows for good generalization of our ECG findings.

Other limitations must be considered. The NRMI database does not contain measures for infarct size determinations; therefore, we could not incorporate these variables into the model. Many patients did not have ejection fractions determined during hospitalization. The use of additional ECG leads was used in only 0.8% of patients; however, right-side leads are primarily used to detect right ventricular infarction associated with inferior ST-segment elevation[37] and posterior leads are unlikely to show significant abnormalities in the absence of anterior ST-segment depression.[38] Newer technologies, such as continuous ST-segment monitoring, facilitate the diagnosis of AMI,[39] but these technologies were not considered herein. Finally, we were unable to perform a competing risk analysis of our composite end point due to data limitations.

In 1998, more than 5.3 million patients sought emergency care for chest pain or related symptoms.[40] In many centers, "low-risk" chest pain patients are evaluated in emergency department–based chest pain units.[41,42] The initial ECG is the first and most effective tool used for risk-stratification of patients with symptoms suggestive of AMI.[43] It is therefore important to understand its prognostic value and to be aware of the actual absolute risks for those patients with proven AMI. Our results underscore the finding that the favorable prognosis of a normal ECG in chest pain patients is not conferred

Table 6. Propensity Matched Samples for Normal Diagnostic Electrocardiogram (ECG) Results*

Characteristics	ECG: Normal (n = 29 281)	ECG: Diagnostic (n = 29 281)	*P* Value
Age, mean (SD), y	65.2 (14.5)	65.5 (14.5)	.005
Men	62.3	61.7	.14
White	84.1	83.8	.39
Medical history			
Myocardial infarction	21.1	21.3	.49
Angina	14.8	14.9	.79
Congestive heart failure	9.9	10.3	.07
Percutaneous coronary intervention	10.3	10.2	.82
Coronary artery bypass graft surgery	10.8	11.0	.53
Diabetes	23.7	24.1	.24
Smoker	26.5	25.9	.11
Time of symptom onset to ED presentation, min			
<120	26.7	25.7	.004
120-360	20.8	20.4	.24
>360	18.6	19.0	.24
Data missing	33.9	35.0	.007
Killip class (assessment of heart failure)			
I (none)	88.7	88.5	.41
II (rales/JVD)	11.3	11.5	.41
Ejection fraction†	55	50	<.001
Heart rate on presentation			
<100/min	85.2	84.8	.10
≥100/min	14.2	14.3	.64
Missing	0.6	0.7	.02
Systolic blood pressure on presentation, mm Hg			
<90	1.7	1.9	.14
90-120	14.5	14.3	.63
>120	83.4	83.3	.77
Missing	0.4	0.5	.23
Chest pain on presentation	64.7	63.7	.01
Admitting diagnosis			
Acute myocardial infarction	15.4	15.2	.53
Rule out acute myocardial infarction	36.9	37.0	.92
Unstable angina	20.6	20.8	.48
Other	27.1	27.0	.81
In-hospital mortality	5.7	9.5	<.001

*Data are presented as percentages unless otherwise indicated. ED indicates emergency department; JVD, jugular venus distention. There were 29 281 patients in each group after matching totaling 58 562 cases. Sixteen variables that comprised 28 fields were used as comparisons (this excludes the outcome of mortality). Of the 28 fields, only 5 showed significance at the $P<.05$ level and only 3 were significant at the $P<.01$ level. None of these differences was thought to be of clinical importance, suggesting excellent matching. The same variables were used to match the nonspecific ECG group (n = 91 221) with the diagnostic ECG group (n = 91 221, total 182 442). Although there were more fields with statistically significant differences, they were also thought to be of little clinical importance. The data for the nonspecific and diagnostic ECG matching groups is not presented herein but is available on request.

†Ejection fractions were not used in the matching process and are the unadjusted median values for each matched group.

to those with confirmed AMI, though patients with AMI and a normal or nonspecific initial ECG are at lower risk for in-hospital death or serious complications than those with diagnostic ECGs. Future work will be needed to define optimal management strategies for patients with AMI who present with initially normal or nonspecific ECGs.

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