The Clinical Utility of Postinfarction Risk Prediction*
Performance Perspective of Electrophysiologic and Other Variables

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SA ECG = signal averaged electrocardiography; TIMI = Thrombolysis in Myocardial Infarction Study Group; VF = ventricular fibrillation; VT = ventricular tachycardia

Coronary artery disease (CAD) continues to be the largest single cause of death among North Americans. In particular, mortality associated with myocardial infarction remains high, with in-hospital rates among all-inclusive patient populations ranging from 7 percent in patients younger than 70 years to 35 percent in patients 70 years or older and postdischarge rates in selected study populations averaging 5 percent to 10 percent per year. Reduction of postinfarction risk is a very pressing therapeutic goal in contemporary cardiology practice. This goal remains elusive, however, in part because individual patients at excess risk cannot be identified accurately and targeted for intensive management.

Historically, three major pathophysiologic conditions have been considered most responsible for increased postinfarction risk of death and major morbidity: poor left ventricular systolic function; potential for further myocardial ischemia from underlying CAD; and potential for repetitive ventricular dysrhythm, with or without stimulus by evident ischemia. Understandably, clinical variables and diagnostic tests that detect these pathophysiologic pathways have been evaluated extensively as predictors of excess postinfarction risk.

A major problem with reliance on a single clinical variable for risk prediction is demonstrated in the recent analysis of data from the Thrombolysis in Myocardial Infarction (TIMI) trial population that showed that the positive predictive value of any single risk factor (age 70 years or older, previous infarction, anterior Q wave infarction, atrial fibrillation, rales in more than one lung field, hypotension and sinus tachycardia, female sex, or diabetes) ranged between 6 and 12 percent. In the same study, even a composite variable comprised of four or more of these clinical risk factors had a positive predictive value of only 17 percent.

Many ancillary diagnostic test criteria have also been evaluated as predictors of postinfarction mortality and morbidity risk. Tests based on electrophysiology have been the most frequently used because of the wide availability and safety of electrocardiography and the ability of the heart’s electrical signal to reflect both electrical instability and ischemic substrates.

To gain a comprehensive perspective of their practical utility, we critically reviewed the screening test performance of electrophysiologic and other variables commonly used to predict postinfarction risk. This review involved studies in several thousand patients, from many different centers, and covered a time frame of two decades. These studies were identified by a computerized literature search and scanning of references in relevant articles. The only criterion for study inclusion was adequacy of the original data in allowing application of the standardized analysis techniques described below.

To enhance interpretation and extrapolation of the results of the review, we applied uniform screening test definitions and methodologies to all of the selected original studies (Fig 1). Thus, even if the original publications did not report sensitivity, specificity, positive and negative predictive values, and relative risk, we calculated each of these screening test parameters from the raw data. This approach allowed, we believe, reliable interstudy comparisons and a more accurate overall reflection of the weight of available evidence.

Mortality

In any assessment of CAD, particularly myocardial infarction, survival/mortality is the most important clinical outcome. Data from nine studies relating prognostic variables to mortality were included. Four of these studies retrospectively analyzed data collected primarily for other purposes and five were designed prospectively. The screening tests used were exer-
cise tolerance testing, body surface potential mapping (BSPM), Holter monitoring, signal averaged electrocardiography (SA ECG), and ejection fraction.

Ellestad and Wan were among the first investigators to assess CAD risk retrospectively in the modern era. In 573 subjects followed up for four years, a subgroup of an original test population of 2,700 subjects who underwent electrocardiographic stress tests as part of a routine medical examination or because of suspected or known CAD, these authors showed that a positive test (ST segment depression ≥1.5 mm) was associated with an increased risk of dying. The positive predictive value was 13 percent for the degree of certainty that a positive test response would truly identify an individual who would die. The negative predictive value was 93 percent for the degree of certainty that a negative test response accurately identified the absence of mortality.

In a retrospective analysis of several BSPM repolarization variables thought to reflect electrical instability in 100 consecutive patients with acute Q wave inferior myocardial infarction, Walker et al reported positive predictive values for mortality ranging from 28 to 37 percent (average, 33 percent) over a median follow-up interval of 14 months.

Ambulatory ST segment deviation, with or without ischemic symptoms, has also been tested as a predictor of postinfarction mortality. For example, in a retrospective analysis of 103 postinfarction patients, Gottlieb et al reported that the value of an individual positive test, defined as transient ST change ≥1 min, in predicting 1-year mortality was 30 percent and the negative predictive value was 89 percent.

Tzivoni et al, in a retrospective Holter analysis of 224 selected infarction patients, reported that 74 had transient episodes of ST change compatible with myocardial ischemia during unspecified periods of monitoring. During a 28-month follow-up interval, a positive test, defined as transient ST change ≥1 min, had a predictive value for mortality of only 5 percent. Among the first prospective assessments of postinfarction mortality risk was the study of Théroux et al. They found that a positive exercise test result, defined as progressively severe angina or ST depression at a low workload prior to discharge, gave a 21 percent positive predictive value for death over the course of the subsequent 12 months (Fig 1). The value of a negative stress test in predicting the absence of mortality over the same interval was 98 percent (Fig 1).

In 1983, the Multicenter Postinfarction Research Group reported the results of a prospective study of more than 800 patients with acute myocardial infarction followed up for one year. They confirmed, for the first time, that left ventricular dysfunction and frequent ventricular ectopic beats were independent risk factors for excess mortality following myocardial infarction. Although exact data were somewhat difficult to calculate from the original article, in part because of loss of 36 subjects from follow-up, the individual predictive value of left ventricular ejection fraction <0.4 for subsequent mortality risk was ≤22 percent and the predictive value of ventricular ectopic beat frequency ≥10/h was ≤21 percent. The negative predictive values of the two variables were 93 percent and 90 percent, respectively.

Denniss et al, in 1986, reported the prospective value of advanced SA ECG testing in predicting cardiac mortality among 403 patients following acute myocardial infarction. They found that delayed depolarization, defined as a signal-average QRS duration >140 ms, gave a positive predictive value for mortality of 11 percent over a two-year follow-up period, compared with a positive predictive value of 13 percent for induction of ventricular tachycardia (VT) by programmed stimulation. The value of a negative SA
ECG and inability to stimulate VT in predicting absence of mortality were, in contrast, very high, 97 percent and 96 percent, respectively.\textsuperscript{10} Interestingly, these authors found that inducible VT was not independent of postinfarction SA ECG in relation to postinfarction risk.\textsuperscript{10}

Walker et al\textsuperscript{4} prospectively applied their retrospectively derived BSPM criteria to a test set of 98 consecutive patients with acute Q wave inferior myocardial infarction.\textsuperscript{11} The average positive predictive value of the ST-segment test variables decreased to 19 percent, with a range of 15 percent to 25 percent.\textsuperscript{11} The negative predictive value of the ST variables remained high, however, ranging from 90 percent to 97 percent.\textsuperscript{11}

In a prospective 39-h Holter study of a clinically uncomplicated patient subgroup 4 \pm 1 days postinfarction, Ouyang et al\textsuperscript{2} reported that transient ST change lasting \geq 2 min had a positive predictive value for inhospital mortality of 4 percent and a negative predictive value of 97 percent.

On average, the sensitivity of the above tests of mortality prediction in the postinfarction setting was 59 percent. While the presence of each of the variables was associated with an increased relative risk of death (range, 1.2 to 12.8), the mean positive predictive value was only 21 percent, with a range of 4 percent to 37 percent. The average positive predictive value of the retrospective studies,\textsuperscript{3,4} however, was higher at 26 percent, compared with the mean value of 16 percent for the prospective studies;\textsuperscript{7-11} (Table 1). In contrast, the overall negative predictive value averaged 94 percent within a very narrow range of 89 percent to 98 percent and there was no difference in the mean values for the prospective (94 percent; Table 1) and retrospective (93 percent) studies.

**Sudden Death and Cardiac Dysrhythm**

In all patients with CAD, including those in the postinfarction setting, sudden death accounts for approximately 50 percent of all deaths. In turn, VT or ventricular fibrillation (VF) is thought to be the responsible pathophysiologic state in approximately 75 percent of these sudden-death CAD victims. Thus, serious arrhythmic events, such as sustained VT and VF, are potentially very important outcome variables in the postinfarction period and screening tests for them as surrogate end points for mortality risk continue to be developed and employed.\textsuperscript{10,18-21} Data from five retrospective\textsuperscript{19-21} and six prospective\textsuperscript{10,17-21} studies were available for analysis.

High-frequency and low-amplitude potentials, which delay offset of the QRS on SA ECG recordings, are thought to reflect slow and fractionated conduction—a substrate for repetitive ventricular dysrhythm in underlying myocardium.\textsuperscript{10,18-17,21} Simson\textsuperscript{18} was the first to report the incidence of SA ECG in postinfarction patients. He defined abnormal late potentials as the root mean square voltage of the terminal 40 ms of the QRS <25 \( \mu \)V, using high-pass, bidirectional filtering of averaged X, Y, and Z leads.\textsuperscript{18} Retrospective comparison of 39 postinfarction patients with symptomatic VT and a control group of 27 postinfarction patients without VT produced a test sensitivity of 92 percent, specificity of 93 percent, positive predictive value of 95 percent, and negative predictive value of 89 percent.\textsuperscript{12}

In a further study of postinfarction patients,\textsuperscript{13} 98 with symptomatic VT and 76 without VT, Kanovsky et al\textsuperscript{13} retrospectively compared the performance of their

### Table 1—Prospective Performance of Electrophysiologic and Other Variables as Screening Tests for Postinfarction Mortality*

<table>
<thead>
<tr>
<th>Study and Variable</th>
<th>Deaths/Positive Tests</th>
<th>Deaths/Negative Tests</th>
<th>Relative Risk</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>Positive Predictive Value, %</th>
<th>Negative Predictive Value, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Théroux et al\textsuperscript{4}</td>
<td>ST ETT/pain MPRG\textsuperscript{a}</td>
<td>17/80</td>
<td>3/130</td>
<td>9.2</td>
<td>85</td>
<td>67</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>LV EF &lt;0.4</td>
<td>61/272</td>
<td>40/558</td>
<td>3.1</td>
<td>60</td>
<td>71</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>VED\textsubscript{a} &lt;10/h</td>
<td>35/166</td>
<td>66/664</td>
<td>2.1</td>
<td>35</td>
<td>82</td>
<td>21</td>
</tr>
<tr>
<td>Dennis et al\textsuperscript{10}</td>
<td>EPS VT</td>
<td>10/80</td>
<td>12/323</td>
<td>3.4</td>
<td>45</td>
<td>82</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>SA ECG</td>
<td>9/80</td>
<td>7/226</td>
<td>3.6</td>
<td>56</td>
<td>76</td>
<td>11</td>
</tr>
<tr>
<td>Bell et al\textsuperscript{11}</td>
<td>BSPM</td>
<td>10/40</td>
<td>4/58</td>
<td>3.6</td>
<td>71</td>
<td>64</td>
<td>25</td>
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<tr>
<td></td>
<td>BSPM</td>
<td>13/83</td>
<td>1/15</td>
<td>2.3</td>
<td>93</td>
<td>17</td>
<td>16</td>
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<tr>
<td></td>
<td>EPSVF</td>
<td>4/27</td>
<td>7/71</td>
<td>1.5</td>
<td>29</td>
<td>76</td>
<td>15</td>
</tr>
<tr>
<td>Ouyang et al\textsuperscript{2}</td>
<td>ST Holter</td>
<td>1/27</td>
<td>1/32</td>
<td>1.2</td>
<td>50</td>
<td>54</td>
<td>4</td>
</tr>
</tbody>
</table>

*BSMP = body surface potential map; EF = ejection fraction; EPS = electrophysiologic study; ETT = exercise tolerance test; MPRG = Multicenter Postinfarction Research Group; SA ECG = signal averaged electrocardiogram; VT = ventricular tachycardia; VED\textsubscript{a} = mean rate of ventricular ectopic depolarizations.*
original SA ECG criterion\textsuperscript{14} with another definition of abnormal SA ECG (QRS duration $\geq 120$ ms), as well as a combination of both SA ECG criteria. Moreover, they evaluated several other predictive criteria, including two definitions of abnormally frequent ventricular ectopic beats, left ventricular ejection fraction $<0.4$, presence of left ventricular aneurysm and a composite variable of any SA ECG, peak ectopic frequency $>100$ h, and presence of aneurysm. In this retrospective study, the positive predictive values of the single and combined electrophysiologic and mechanical variables ranged from 76 percent to 100 percent.

Interestingly, multivariate logistic regression analysis revealed that the SA ECG criteria, peak ectopic frequency $>100$ h, and presence of left ventricular aneurysm were independently associated with the greatest increased relative risk for VT.\textsuperscript{13} Thus, it is not surprising that the combination of all three of these individual variables in a composite variable increased the positive predictive value to 100 percent for this retrospective analysis.\textsuperscript{13}

Other retrospective studies of SA ECG in prediction of postinfarction cardiac dysrhythmia\textsuperscript{14,15} have produced compatible test results, considering the relatively low incidence of VT (18 percent) in the postinfarction patients whose cases were reported by Hanashima et al\textsuperscript{14} and that the control group in the study of Faguere et al\textsuperscript{16} were normal subjects.

Retrospective BSPM studies\textsuperscript{14,16} have also given compatible screening test results for prediction of VT and VF in postinfarction patients (Table 2). These include measures of early, as opposed to late, QRS activation delay\textsuperscript{14} and irregular, multipolar isointegral QRST maps, the latter a reflection of increased disparity of ventricular primary repolarization properties.\textsuperscript{16} None of the BSPM variables has been studied prospectively in postinfarction risk prediction.

Prospective single variable studies of postinfarction arrhythmic risk\textsuperscript{10,12-15} have yielded much lower positive predictive values, on average 21 percent (Table 2), compared with the retrospective studies,\textsuperscript{16-16} on average 73 percent. Moreover, the range of positive predictive values in the prospective studies has been narrow (7 percent to 38 percent) and there were no real differences among the several individual variables.

\begin{table}[h]
\centering
\begin{tabular}{|l|c|c|c|c|c|c|c|}
\hline
\textbf{Study} & \textbf{Events/Variable} & \textbf{Positive} & \textbf{Events/} & \textbf{Negative} & \textbf{Relative} & \textbf{Sensitivity, } & \textbf{Specificity,} & \textbf{Positive} & \textbf{Negative} \\
\hline
\textbf{Denniss et al}\textsuperscript{14} & SA ECG & 15/90 & 8/226 & 5.3 & 65 & 77 & 19 & 96 \\
 & EPS VT & 14/90 & 13/323 & 4.3 & 52 & 96 & 18 & 96 \hline
\textbf{Kuchar et al}\textsuperscript{15} & SA ECG & 13/78 & 2/122 & 10.2 & 87 & 65 & 17 & 98 \\
 & VED\textsubscript{10} & 1/15 & 14/191 & 0.9 & 7 & 93 & 7 & 93 \\
 & LV EF $<0.4$ & 13/64 & 2/146 & 14.8 & 87 & 74 & 20 & 99 \\
 & SA ECG + EF & 12/35 & 3/165 & 18.9 & 80 & 88 & 34 & 98 \hline
\textbf{Gomes et al}\textsuperscript{16} & SA ECG & 10/26 & 6/89 & 5.7 & 63 & 84 & 38 & 93 \hline
 & VED & 13/47 & 3/47 & 4.3 & 81 & 56 & 28 & 94 \hline
 & LV EF $<0.4$ & 12/56 & 4/54 & 2.9 & 75 & 53 & 21 & 93 \hline
\textbf{Gomes et al}\textsuperscript{17} & SA ECG & 13/45 & 2/57 & 7.3 & 87 & 63 & 29 & 96 \hline
 & LV EF $<0.4$ & 12/50 & 3/47 & 4.0 & 80 & 49 & 24 & 91 \hline
 & VED\textsuperscript{1} & 12/52 & 3/32 & 2.6 & 23 & 42 & 23 & 91 \\
 & SA ECG + VED & - & - & - & - & - & - & - \\
\textbf{El-Sherif et al}\textsuperscript{18} & SA ECG & 9/39 & 3/117 & 7.7 & 75 & 79 & 23 & 97 \hline
 & LV EF $<0.4$ & 8/51 & 4/83 & 3.2 & 67 & 65 & 16 & 95 \\
 & VED\textsuperscript{1} & 6/43 & 6/107 & 2.3 & 50 & 73 & 14 & 94 \hline
 & SA ECG + VED & - & - & - & - & - & - & - \\
\textbf{Kuchar et al}\textsuperscript{19} & SA ECG & 16/91 & 12/152 & 2.2 & 57 & 65 & 18 & 92 \\
\hline
\end{tabular}
\caption{Prospective Performance of Electrophysiologic and Other Variables as Screening Tests for Postinfarction Arrhythmic Events (Sudden Death, VT or VF)\textsuperscript{a}}
\end{table}

\textsuperscript{a}VED\textsubscript{1} = peak ventricular ectopic rate; VED\textsubscript{1} = repetitive VEDs; VED\textsubscript{1} = frequent ($>10$h) or repetitive ventricular ectopic depolarizations. Other abbreviations are expanded in Table 1 footnote.
although frequent isolated ectopic activity has performed particularly poorly\textsuperscript{17} (Table 2). This may not be a moot point, considering the dichotomy between frequent ectopic activity and subsequent clinical outcome in the recent postinfarction Cardiac Arrhythmia Suppression Trial (CAST).\textsuperscript{12}

Three prospective studies have also evaluated composite variables.\textsuperscript{17,19,20}

Kuchar et al\textsuperscript{17} followed up 210 patients for a median of 14 months and found, by logistic regression, that SA ECG and left ventricular ejection fraction <0.4 were independent predictors of excess risk. When combined in a composite variable where a positive test required the presence of both, Kuchar et al reported a positive predictive value of 34 percent, compared with 7 percent to 20 percent when the individual variables were evaluated separately\textsuperscript{17} (Table 2).

Gomes et al\textsuperscript{10} have also reported that SA ECG, repetitive ventricular ectopic activity, and ejection fraction <0.4 were all independently associated with high relative risks for an arrhythmic event. In another study using combinations of two or all three of these variables, Gomes and coworkers\textsuperscript{19} have reported positive predictive values ranging from 35 percent to 50 percent (Table 2). Using similar composite variables as a positive cumulative index or test, El-Sherif et al\textsuperscript{20} reported positive predictive values from 27 percent to 57 percent. El-Sherif et al\textsuperscript{20} also reported that timing of the tests could substantially affect test performance, with assessments done 6 to 30 days postinfarction having the highest predictive values.

In both of these latter studies, consecutive patients were not evaluated and all tests were not used in all enrolled patients.\textsuperscript{19,20} Thus, accurate measures of test sensitivity could not be calculated (Table 2). This is unfortunate since, although predictive value increased relative to single variable testing (Table 2), decreased sensitivity would be a companion expectation and it is important to know to what degree this is manifest before composite testing can be considered practical.

Most recently, Kuchar et al\textsuperscript{21} reported the long-term performance of SA ECG screening in 243 postinfarction patients followed up for 5 years (Table 2). They found a positive predictive value of 18 percent and a negative predictive value of 92 percent (Table 2). Thus, these long-term follow-up data are very similar to the previous shorter-term prospective data (Table 2) and confirm that if postinfarction SA ECG testing is negative prior to discharge, there is a low risk of developing a clinically severe cardiac dysrhythm event for up to 5 years postdischarge (Table 2).\textsuperscript{21}

### Reinfarction

The prediction of reinfarction risk following an index myocardial infarction has received surprisingly little specific attention. Limited data from four studies (two retrospective and two prospective) are available.\textsuperscript{6,23-25} This is unfortunate, considering the increasing overall incidence of non-Q-wave infarction\textsuperscript{25} and the increasing use of thrombolytic therapy in patients with Q-wave infarction.\textsuperscript{26} In both of these clinical presentations of CAD, that is non-Q-wave and lytic-treated Q-wave infarction, there is a strikingly increased relative risk of reinfarction.\textsuperscript{25,26}

The common denominator in non-Q-wave and lytic-treated Q-wave infarctions is an infarct-related artery pathophysiologic condition that is associated with high rates of early patency and late complications, particularly reinfarction.\textsuperscript{25,26} The reason for the increased reinfarction risk in these infarct settings can only be speculated at this time. Nevertheless, it seems reasonable to assume the acute infarct related artery has some unstable balance of prothrombotic and prolytic factors that, with time, results in an enhanced risk of the balance tipping toward thrombotic occlusion and reinfarction.

In a previous extensive comparison of the clinical features of Q-wave and non-Q-wave infarction, we found the rate of reinfarction among non-Q-wave infarction patients to average 12 percent (range, 8 percent to 43 percent) over follow-up intervals of ≤1 month to 30 months, compared with an average risk of 6 percent (range, 2 percent to 8 percent) for patients with Q-wave infarction followed up for the same intervals.\textsuperscript{25} Assuming a Q-wave to non-Q-wave incidence ratio of 4:1, which is the reported average in continuous series of infarction patients,\textsuperscript{25,27,28} the average predictive value of non-Q-wave myocardial infarction as a screening test for reinfarction risk should be approximately 21 percent.

Relevant to the above data is evidence from a prospective study of the utility of fibrinolysis variables in characterizing postinfarction risk of reinfarction.\textsuperscript{29} Similar results were reported in a recent placebo-controlled study of intravenous streptokinase,\textsuperscript{30} a fibrinolysis variable, in which the average positive predictive value of non-Q-wave myocardial infarction was 44 percent, compared with 8 percent for Q-wave myocardial infarction.
Gram and colleagues measured tissue plasminogen activator activity in plasma euglobulins of 29 consecutive infarct patients as areas of lysis on fibrin plates and reported significantly lower levels at eight weeks' postinfarction in patients who had a subsequent reinfarction. The positive predictive value of plasminogen activator activity ≥16 sq mm was very high, 53 percent, despite a relatively low overall incidence of reinfarction during the four-year follow-up (Table 3).

Other relevant data implicating the coagulation/anticoagulation balance in the infarct-related artery to subsequent reinfarction risk are less direct, but nevertheless compelling. Individual clinical trials and overview analyses have incontrovertibly demonstrated that antiplatelet and other agents that interrupt the coagulation cascade markedly reduce the risk of reinfarction in patients with acute myocardial infarction, both in the presence and absence of thrombolytic therapy. Thus, the hematologic, at least the thrombolytic, coagulation and anticoagulation factors cannot be neglected in terms of postinfarction risk prediction.

The total number of diseased coronary vessels may also be an important factor in subsequent reinfarction risk. Sanz et al reported the results of a prospective multivariate analysis in 403 consecutive infarction patients followed up for almost six years. They found the positive predictive value of ≥2-vessel CAD for reinfarction was 18 percent, with a negative predictive value of 95 percent (Table 3).

Lastly, symptomatic and asymptomatic ST-segment changes have also been evaluated as a risk predictor for reinfarction, although in the retrospective study of Tzivoni et al, the predictive value of a positive test was only 11 percent.

Conclusions

There are three major conclusions from this review.

First, the data are remarkably consistent, qualitatively and quantitatively, despite the heterogeneity of tests, study populations, time frames, and end points evaluated.

Second, in the postinfarction setting, individual negative predictive tests have relatively high degrees of accuracy, approximately 90 percent, in forecasting absence of subsequent risk (Tables 1 to 3).

Third, reliable prospective identification of the presence of risk is, on the other hand, far less than optimal, averaging about 20 percent for prediction of death or serious arrhythmia (Tables 1 to 3), despite the association of many individual variables with increased relative risk. In other words, a patient identified to be in the higher-risk group by virtue of a positive test response has, nevertheless, an 80 percent chance of uneventful survival.

Patients die or develop major complications such as VT or VF and reinfarction via a number of mechanisms, some known, others yet unknown. Because of the multiplicity of potential pathophysiologic pathways, and our present uncertain knowledge of their exact mechanisms, it may be unreasonable to expect that any single prospective assessment of risk would be sufficiently powerful to have a positive predictive value much greater than 20 percent. The results of this review certainly support this view.

A composite variable reflecting several independent pathophysiologic pathways of risk is, therefore, attractive. Such an approach might reasonably be expected to significantly increase clinical risk prediction, not only because such a variable would encompass a greater number of pathways for postinfarction mortality and morbidity, but also because it could be made inclusive. That is, all component variables would have to be present for the composite to be considered positive and false positive responses would be reduced. As a corollary, aggressive investigation and therapy in low- and moderate-risk patients would also be reduced.

In previous studies that considered a composite of individual variables as risk predictors, the positive predictive values tended to increase, although not invariably so, and the effects on test sensitivity remain uncertain. In the most recent prospective clinical trial of a β-blocker, in what was designed to be an evaluation of proven effective medical therapy in a high-risk infarction population, the use of a composite variable comprising several clinical risk factors did not prevent the study from being prematurely terminated because the control mortality was unexpectedly low (11 percent vs a predicted 20 percent). The best performances of composite variable prediction have been for arrhythmic events, in the range of 40 percent to 50 percent. Thus, 50 percent to 60 percent of the contribution to postinfarction risk, even in the best case situation, remains beyond our present abilities to detect.

The analysis of this review did not involve any formal considerations of intercurrent therapy and almost all the studies were completed prior to the widespread adoption of acute thrombolytic therapy for myocardial infarction. Nevertheless, the high false positive rate may have been determined in some measure by medical therapies and may even be further influenced by thrombolysis. A major clinical implication for the foreseeable future, in the continuing absence of the reliable separation of those patients truly positive from those with only false positive tests, is that physicians and health care administrators concerned with reducing excess myocardial infarction risk will have to be content with the inherent inefficiency of applying effective or promising therapy to all patients or at least all patients testing positive on standard risk evaluation assessments.

Further studies to better elucidate the pathophysi-
ology of infarction and reinfarction are necessary if prognostic assessment and therapy are to advance.

References


