Risk stratification for 1 year survival based on characteristics identified in the early hours of acute myocardial infarction

The Western Washington Intracoronary Streptokinase Trial

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ABSTRACT We evaluated the relationship between baseline factors defined at 4.6 ± 2.1 hr after onset of acute myocardial infarction and 1 year survival in 245 patients entered in the Western Washington Intracoronary Streptokinase Trial. Univariate statistics identified a significant relationship between 10 of these factors and survival. Multivariate analysis identified three factors as being most closely related to survival: (1) left ventricular ejection fraction (LVEF) (p < .0001), (2) treatment with streptokinase (p = .03), and (3) location of infarction (p = .04). Mathematic models based on this analysis and applied to our patients identified high- and low-risk subgroups for 1 year mortality. Patients receiving standard, not interventional, therapy with anterior infarction and an LVEF of 50% or less and those with inferior infarction and an LVEF of 39% or less comprised the high-risk group. For patients receiving standard therapy, 1 year mortality was 41% in the high-risk group and 4% in the low-risk group. The models illustrated the magnitude of benefit of streptokinase treatment and achievement of complete reperfusion for those at low and high risk. We conclude that LVEF determined in the first hours of acute myocardial infarction is the most important of all baseline factors for prediction of 1 year survival. Mathematic models based on left ventricular function measured as ejection fraction are useful for risk stratification in this setting.  

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THE RISK for recurrent cardiac events in the year after an acute myocardial infarction has been the subject of many investigations.1-10 These studies have demonstrated that certain patient characteristics permit the definition of high- and low-risk subgroups for recurrent cardiac events. Typically, risk assessment was performed at the time of hospital discharge,3-10 although several groups have applied the concept of risk assessment during the first 24 hr of hospitalization.1,2

Interventional therapies in the first hours of acute myocardial infarction have been applied in hopes of decreasing infarct size and improving subsequent survival.11-18 Because the myocardial infarction process is progressive over time,17,18 patients must be selected for interventional therapy at the time of hospitalization. The concept of risk stratification may also be applicable in this setting. If high- and low-risk subgroups for subsequent mortality can be defined at the time of hospitalization, the relative risk for subsequent mortality in a given patient can be balanced against the risks and potential benefits of interventional therapy.

In this report, we evaluate the relationship between 1 year survival outcome and patient historical, clinical, and angiographic characteristics identified a mean of 4.6 ± 2.1 hr after the onset of acute myocardial infarction in 245 patients. From this analysis, models defining probability of 1 year survival are developed. Application of these models in our population demonstrates their usefulness as prognostic devices for risk stratification in the first hours of acute myocardial infarction.

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Methods

The prognostic models developed in this study are based on data acquired in the Western Washington Randomized Intracoronary Streptokinase Trial, the organization and results of which have been reported in detail previously.16–23 Pertinent to this report, all eligible patients were 75 years of age or younger, and they had symptoms and typical electrocardiographic findings of acute myocardial infarction. They were without other life-limiting illness and had not required treatment for congestive heart failure before the entry event. All patients consented to enter this study using forms approved by our institutional Human Subjects Review Committee. Baseline clinical and electrocardiographic characteristics were recorded, then the patient underwent 30 degree right anterior oblique left ventricular angiography followed by coronary angiography. If coronary artery occlusion or subtotal occlusion with thrombosis was identified, patients were randomly allocated to routine coronary care or intracoronary infusion of streptokinase. Patients without angiographic characteristics of coronary thrombosis were not enrolled in this trial. Two hundred fifty patients were enrolled; 116 were assigned to the control group and 134 to the streptokinase group. Mortality was determined in all patients at 30 days, 6 months, and 1 year.

Factors related to 1 year survival include patient historical characteristics, location of ST segment elevation on admission electrocardiogram (ECG), patient clinical profile at the time of catheterization, and the results of a prospective analysis of coronary and left ventricular angiographic data. Location of ST segment elevation on admission ECG was classified as anterior if present in leads V1 to V5, I, or aVL and as inferior if present in leads II, III, or aVF. Coronary angiograms from 245 patients were available for prospective analysis in the central laboratory; 227 of these studies had technically adequate left ventricular angiograms for quantitative analysis.21 These contrast studies were reviewed and quantitated by investigators and technicians blinded to patient survival outcome. Global left ventricular ejection fraction (LVEF) was calculated by the area-length method.24 Three variables of regional left ventricular function were determined by the centerline technique25, 26; these included the akinetic segment (the percentage of left ventricular perimeter with akinesis and/or dyskinesis), the hypokinetic segment (the percentage of left ventricular perimeter with hypokinesis, akin- nesis, or dyskinesis), and the presence or absence of hyperkinesis (see ref. 23 for detailed explanation of these measurements). Coronary angiograms were analyzed for the following information: (1) location of the infarct-related occlusion in the coronary bed, (2) extent of collateral blood flow to the infarct bed, (3) percent diameter stenosis of the infarct-related vessel on initial injection of contrast agent, and (4) in patients receiving streptokinase, the response to thrombolytic therapy. Complete reperfusion was defined as normal or nearly normal flow in the treated vessel distal to the initial occlusion, partial reperfusion was defined as incomplete filling and/or delayed washout of the distal vessel, and no reperfusion was defined as the absence of contrast in the distal vessel after treatment.20

Statistical methods. Mean values are expressed as ± 1 SD. The relationship of individual baseline factors (variables) to 1 year survival was tested by chi-square and two-sided t tests. The .05 level was used to determine statistical significance. Reported p values should be considered nominal because of the post hoc nature of this analysis. Stepwise logistic regression was used to select variables that were the most closely related to 1 year survival.22 Selected variables and coefficients were used in a logistic regression model to determine an equation for estimating the probability of surviving 1 year, and the equation was validated by the cross-validation method.23 An operating characteristic curve29 was used to evaluate cutpoints after compari- son of predicted (by the model) and observed outcome in our population. In these comparisons, sensitivity was the proportion of patients who died who were classified as high risk, and specificity was the proportion of survivors who were classified as low risk.

Results

This analysis is limited to the 245 patients who had central review of their angiographic data. Mean patient age was 56.5 ± 10.6 years; 86% were men and 13% had a history of prior acute myocardial infarction. Mean time to complete acquisition of baseline data (including coronary and left ventricular angiography) was 4.6 ± 2.1 hr after onset of symptoms. At 1 year after entry, 28 patients had died. Twenty-six deaths were classified as cardiac events, one as a probable cardiac event, and one as a noncardiac event.20

Univariate analysis. Results of the univariate analysis of the relationship between baseline variables identified in the first 12 hr of acute myocardial infarction and 1 year survival are shown in table 1. Total 1 year mortality was used in this analysis. From patient history, survivors were younger (55.9 ± 10.5 vs 60.5 ± 11.0 years; p = .03) and had a less frequent history of prior acute myocardial infarction (11% vs 30%; p = .03) than those who died. Location of ST segment elevation was highly related to outcome; 82% of those who died had anterior ST segment elevation (p < .0001 for anterior vs inferior ST location). Three clinical factors identified at the time of catheterization were related to outcome: hypotension with systolic blood pressure under 90 mm Hg (14% prevalence in survivors vs 29% in nonsurvivors; p = .05), pulmonary edema (4% in survivors vs 14% in nonsurvivors; p = .01), and cardiogenic shock (1% in survivors vs 11% in nonsurvivors; p = .003). Presence of continuing chest pain at the time of catheterization and necessity for prior defibrillation were not related to outcome. Data on two other variables, moribund status and use of an intra-aortic balloon pump, were collected but not used in this analysis. Moribund status was defined subjectively and thus was potentially not reproducible; an intra-aortic balloon pump was used in only one patient in this study.

Outcome was significantly related to factors identified by angiography. One year mortality was 20% in those with left anterior descending artery (LAD) thrombosis, 4.5% in those with right coronary artery (RCA) thrombosis, and 0% in 20 patients with circumflex artery thrombosis (p = .0003). Global LVEF was 51 ± 10% in survivors and 35 ± 12% in nonsurvivors (p < .0001). Likewise, akinetic segment and hypokinetic segment were shorter in survivors (for akinetic
For the group achieving complete reperfusion with intracoronary streptokinase, 1 year mortality was 2.5%; for those with partial reperfusion after treatment, mortality was 23%; for those with no reperfusion after streptokinase, mortality was 15% (p = .008).

**Multivariate analysis.** Data on all variables listed in table 1 were available in 219 patients, allowing application of multivariate analysis in this group; 18 of the total 245 patients had no suitable left ventricular angiogram for quantitative analysis and eight other patients had one or more missing clinical variables. Twenty-six deaths occurred in this group of 219 patients. Global LVEF determined a mean of 4.6 hr after onset of symptoms entered the analysis at the first stage and was very powerfully related to outcome (p < .0001). Two other factors, streptokinase treatment (p = .03) and the location of thrombosis in the LAD (p = .04), were also related to outcome. Of the variables not related to outcome in this multivariate analysis, one deserves special comment. Location of ST segment elevation on initial ECG closely corresponds to location of thrombosis in the coronary arteries by angiography. In the stepwise multivariate analysis, after entry of angiographic location of thrombosis (F = 5.06), the F statistic for location of ST segment elevation fell from 4.84 to 0.08. This suggests that location of thrombosis in the coronary bed and the location of ST segment elevation have similar relationships to outcome.

By means of logistic regression analysis, a mathematical model relating LVEF, location of infarction, and potential use of streptokinase was developed. The model and the coding for significant variables is shown in Appendix 1. Probability of survival (P) calculated from the model will be large (near 1.0) for patients who are likely to survive 1 year and small (near 0) in those who are likely to die within 1 year. To evaluate the model’s operating characteristics, we applied it in the population from which it was derived. Posterior probability of survival was calculated from the model for each of the 219 patients in this analysis. This posterior probability was then compared with observed outcome. The operating characteristic curve in figure 1 illustrates the sensitivity and specificity for observed values of P in this comparison. We used this operating characteristic curve to aid in the selection of a cutoff. Selection of cutpoints can be based on a number of different factors, for instance cost analysis or minimizing total number of errors. We wanted to select the cutpoint that optimally separated 1 year survivors from those that died, thus we chose the p value (p = .89)

### Table 1

Table 1: Univariate relationship between baseline variable and 1 year survival

<table>
<thead>
<tr>
<th>Patient history</th>
<th>Survivors</th>
<th>Deaths</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>55.9 ± 10.5</td>
<td>60.5 ± 11</td>
<td>.03</td>
</tr>
<tr>
<td>% Male</td>
<td>87</td>
<td>79</td>
<td>.22</td>
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<tr>
<td>History of prior AMI (%)</td>
<td>11</td>
<td>30</td>
<td>.03</td>
</tr>
<tr>
<td>Time to admission (hr)</td>
<td>2.1 ± 2.0</td>
<td>2.7 ± 3.0</td>
<td>.15</td>
</tr>
<tr>
<td>Admission ECG (n = 237)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior ST elevation</td>
<td>91</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Inferior ST elevation</td>
<td>118</td>
<td>5</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Clinical status at cath.</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Ongoing chest pain (%)</td>
<td>88</td>
<td>89</td>
<td>.94</td>
</tr>
<tr>
<td>Hypotensive &lt; SBP 90 (%)</td>
<td>14</td>
<td>29</td>
<td>.05</td>
</tr>
<tr>
<td>Pulmonary edema (%)</td>
<td>4</td>
<td>14</td>
<td>.01</td>
</tr>
<tr>
<td>Cardiogenic shock (%)</td>
<td>1</td>
<td>11</td>
<td>.003</td>
</tr>
<tr>
<td>Status post defibrillation (%)</td>
<td>10</td>
<td>18</td>
<td>.22</td>
</tr>
<tr>
<td>Coronary anatomy</td>
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<td>Infarct-related vessel</td>
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<tr>
<td>LAD</td>
<td>91</td>
<td>23</td>
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</tr>
<tr>
<td>RCA</td>
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<td>5</td>
<td>.0003</td>
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<td>CIRC</td>
<td>20</td>
<td>0</td>
<td></td>
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<tr>
<td>Initial subtotal occlusion of infarct-related vessel (%)</td>
<td>15</td>
<td>14</td>
<td>.89</td>
</tr>
<tr>
<td>Collateral present to infarct bed (%)</td>
<td>31</td>
<td>20</td>
<td>.27</td>
</tr>
<tr>
<td>LV function (n = 227)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>LVEF (%)</td>
<td>51 ± 10</td>
<td>35 ± 12</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Akinetic segment (% of LV perimeter)</td>
<td>9 ± 11</td>
<td>21 ± 14</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Hypokinesis segment (% of LV perimeter)</td>
<td>27 ± 14</td>
<td>46 ± 17</td>
<td>&lt;.0001</td>
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<tr>
<td>Hyperkinesis present (%)</td>
<td>34</td>
<td>19</td>
<td>.14</td>
</tr>
</tbody>
</table>

AMI = acute myocardial infarction; LAD = left anterior descending artery; RCA = right coronary artery; CIRC = circumflex artery; LV = ventricular; SBP = systolic blood pressure.
close to the 100% sensitivity, 100% specificity point in figure 1. For \( p \leq .89 \), the model correctly identified 21 of 26 patients dying (81% sensitivity); for \( p > .89 \), the model correctly identified 147 of 193 surviving patients (76% specificity).

The model was validated by applying it in the population from which it was derived with the cross-validation method. Since a cross-validation program for logistic regression was not available to us, the data were reexamined by discriminant analyses. With the observed mortality rate as the prior probability, the number of patients classified as dead and alive was the same with and without the cross-validation method. The discriminant function for the prognostic model was very similar to the function estimated by the logistic regression. Sensitivity and specificity for the \( p = .89 \) cutpoint by the discriminant function were also nearly identical to values here for the logistic regression analysis. This indicates that a similar result would hold for a cross-validation logistic regression analysis.

The model’s outcome for different combinations of the predictor variables is illustrated in figures 2 to 4. In figure 2, the effects of different LVEFs on survival in patients who received standard therapy (i.e., no intracoronary streptokinase) is shown. The probability cutpoint value with maximal sensitivity and specificity for separating survivors from nonsurvivors is indicated.

This value divides the curves into two regions, one indicating a low risk of death in follow-up and the other indicating a high risk of death. For patients with anterior infarction, those with an LVEF of 50% or less are in the high-risk group for death in the first year after acute myocardial infarction. In the Western Washington Randomized Intracoronary Streptokinase Trial, 69% of patients with anterior infarction were in this high-risk group. For those with inferior infarction, patients with an LVEF of 39% or less are required to be in the high-risk group for death. Only 9% of patients with inferior infarction in the Western Washington Trial were in the high-risk group.

The effect of streptokinase treatment in relationship
to LVEF and location of infarction is illustrated in figures 3 and 4. For patients with anterior infarction, the model shows a beneficial effect of streptokinase on survival at all values of LVEF (figure 3). However, clinically relevant benefit is probably restricted to a smaller portion of the patient population. Patients with an LVEF greater than 50% are at low risk for 1 year mortality with standard treatment. Benefit in terms of improved probability of survival is also small with intracoronary streptokinase treatment in this group. Mean improvement in probability of survival (calculated as P [streptokinase treatment] – P [standard treatment] for a given LVEF × 100, expressed as percent) in this low-risk group is 3.5% (range 1.0% to 6.6%). Patients with anterior infarction and LVEF of 50% or less are at much higher risk of 1 year mortality with standard treatment. Probability of improved survival with streptokinase treatment is also greater in this group compared with the low-risk group. Mean improvement in probability of survival with streptokinase in this high-risk group is 18% (range 7% to 27%). Similar conclusions can be drawn from analysis of standard and streptokinase treatment curves in inferior acute myocardial infarction (figure 4). Thus patients with a low risk of 1 year mortality by standard treatment have a small improvement in probability of survival with streptokinase treatment. High-risk patients with standard treatment have a much larger improvement in probability of survival with streptokinase treatment than do those in the low-risk group.

This conclusion can be illustrated by applying this analysis to observed outcome in the Western Washington Trial population. Of 102 patients receiving standard therapy in this trial who had baseline LVEFs, 34 would have been classified as high risk and 68 as low risk by application of this analysis. One year mortality was 41% (14/34 patients died) in the high-risk group and only 4.4% (3/68) in patients who would have been classified as low risk. For the 124 patients receiving streptokinase who had baseline LVEFs, 47 would have been classified as high risk and 77 as low risk. One year mortality was 19% (9/47) in the streptokinase group high-risk patients and only 1.3% (1/77 patients) in the low-risk patients. Thus mortality was reduced from 41% with standard care in high-risk patients to 19% by streptokinase treatment in high-risk patients (p = .03). For low-risk patients, 1 year mortality was low with standard care and although there was trend toward lower mortality in low-risk patients treated with streptokinase, this trend did not reach statistical significance (p > .1).

We have previously emphasized the important relationship between achievement of complete reperfusion in streptokinase-treated patients and 1 year outcome. Survival benefit was limited to those with complete reperfusion; 1 year mortality was significantly higher in those with either partial or no reperfusion after streptokinase treatment. To evaluate the importance of reperfusion status relative to other baseline variables already discussed, multivariate analysis was performed in the group receiving streptokinase therapy entering reperfusion status in addition to baseline variables listed in table 1. In this analysis, LVEF (p = .002) entered at the first stage of the model and reperfusion status after streptokinase (p = .03) entered second. By logistic regression analysis, a second mathematic model relating LVEF, reperfusion status, and location of infarction to 1 year survival was developed (Appendix 2). The effect of reperfusion status relative to standard treatment and streptokinase treatment without consideration of reperfusion status is also shown in figures 3 and 4. Achieving complete reperfusion with treatment dramatically improves probability of survival compared with standard treatment in those at high risk. The survival curves for those with no reperfusion or partial reperfusion were very similar to the standard treatment curves and were not drawn in these figures.

Decisions to perform coronary artery bypass surgery or percutaneous transluminal coronary angioplasty were made on clinical grounds in this trial. Interim coronary bypass or coronary angioplasty status was known in 226 patients with baseline left ventricular angiograms suitable for quantitative analysis. Bypass
surgery or angioplasty was performed in 37 of 149 patients (25%) who would have been classified low risk by this analysis and in 20 of 77 patients (26%) who would have been classified high risk. There were no procedure-related deaths in patients undergoing coronary bypass surgery or coronary angioplasty in this trial. Conclusions about the usefulness of these procedures for influencing survival in low- and high-risk patients cannot be made from our data.

Discussion

This study defines the relationship between patient characteristics in the first hours of acute myocardial infarction and subsequent 1 year survival. The results of this study apply best to patients who are similar to those evaluated here. In general, these patients were relatively young (men age 56 ± 11 years), were having their first acute myocardial infarction (only 13% had a history of prior acute myocardial infarction), and had not been treated for congestive heart failure before onset of the entry event. These patients did not have known life-limiting illnesses other than the acute myocardial infarction and had no contraindication to thrombolytic therapy. All patients had ST segment elevation on their entry ECGs. We think that these characteristics define a population of patients that is ideal for consideration for interventional therapy in the first hours of acute myocardial infarction.

Our analysis is consistent with the findings of others who have studied the relationship between factors present in the first day of acute myocardial infarction and subsequent 1 year mortality. Patient age,1 2.30 history of prior acute myocardial infarction,1 2.30 indirect manifestations of larger infarct size such as hypotension and pulmonary edema,1 2.30 and anterior location of infarction by ECG32.33 can all be defined in the first hours of the event and have been previously found to be associated with higher subsequent mortality. We have found the same results in this study. Most importantly though, we have found that a direct measurement of left ventricular function, the LVEF obtained within hours of onset of the acute myocardial infarction, is the most powerful predictor of subsequent 1 year outcome.

Forrester et al.34 and Wolffenbuttel et al.35 have shown that risk stratification can be performed 1 to 2 days after onset of acute myocardial infarction by invasively determined hemodynamic variables that reflect extent of left ventricular dysfunction. Many studies have evaluated the relationship between patient characteristics at the time of hospital discharge after acute myocardial infarction and subsequent survival.3 10

Two characteristics, low LVEF and presence of frequent or complex ventricular premature beats, define patients as being at high risk in this late hospital phase setting. Thus patients in the hospital phase of acute myocardial infarction can be divided into low- and high-risk groups for subsequent survival based on definable characteristics primarily related to the extent of left ventricular dysfunction. Our analysis demonstrates that extent of left ventricular dysfunction, measured as LVEF, remains the most important predictor of subsequent outcome when prognosis is assessed within hours of onset of acute myocardial infarction.

Although LVEF was identified as being the factor most closely related to 1 year survival, measures of regional left ventricular function were also closely related to survival in the univariate analysis (table 1). In a similar multivariate analysis with baseline data from this trial and 6 month mortality as an end point, a measure of regional left ventricular function — the hypokinetic segment length — was the baseline factor most closely related to survival.36 These observations suggest that quantitative measures of global and regional left ventricular function obtained in the early hours of acute myocardial infarction carry similar important prognostic information.

Prior investigators have applied one LVEF cutpoint to all patients with acute myocardial infarction for the purposes of risk stratification.30 37 Our analysis has resulted in two LVEF cutpoint values, 50% in patients with anterior AMI and 39% in patients with inferior AMI. Stated another way, patients with inferior infarction receiving standard therapy who had an LVEF between 39% and 50% had a better prognosis than patients with anterior AMI who had LVEFs in the same range in our study. There are several potential explanations for this observation. Infarct expansion and left ventricular aneurysm formation have been associated with poorer prognosis in patients with acute myocardial infarction.38 39 Perhaps there is a greater tendency for infarct expansion or aneurysm formation in patients with anterior acute myocardial infarction and initial LVEFs between 39% and 50% than there is in patients with inferior infarction and LVEFs in the same range. For patients with inferior acute myocardial infarction, two infarctions, the acute event and a prior infarct in another arterial bed, appear to be required to lower the LVEF enough for it to enter the high-risk region of the model. The difference in prognosis between the patients with anterior and inferior acute myocardial infarction with LVEFs between 39% and 50% was not due to an absence of patients with inferior acute myocardial infarction with LVEFs between 39% and 50%.
Thirty-four percent of patients with inferior acute myocardial infarction receiving standard treatment had initial LVEFs between 39% and 50%; 35% of the anterior acute myocardial infarction group receiving standard treatment had LVEFs in this range.

Before further implications of the models developed here are discussed, limitations of this study must be acknowledged. This analysis represents a post hoc approach without antecedent hypothesis. As such, the results of the analysis must be taken with caution. Further validation will require prospective application of the model in another group of patients. The patient population on which the prognostic model is based is relatively small. Only patients who were candidates for interventional therapy and who met strict entry criteria were included in this study. Thus, as was noted above, the model should apply best to patients who are similar to those in the Western Washington Trial. Despite these limitations, the strong predictive value of data obtained very early in the course of infarction is potentially important for the future management of acute myocardial infarction. Although there has been intense interest in interventional therapy in the last 4 to 5 years, invasively determined data obtained in patients receiving standard (not interventional) therapy is quite uncommon. This is the largest series of patients receiving standard therapy for acute myocardial infarction in whom baseline quantitative analysis of left ventricular function has been performed. This series has been large enough to permit evaluation of baseline factors that influence 1 year survival in this type of patient so that a model potentially useful for determining prognosis could be developed.

Optimal implementation of our suggested approach to risk stratification will require noninvasive assessment of left ventricular function when patients first present to the hospital. Radionuclide blood pool imaging is one noninvasive diagnostic method for measurement of LVEF. Correlation between radionuclide and contrast angiographic LVEFs is not perfect, however; in general, radionuclide LVEFs are slightly lower than contrast angiographic LVEFs.\(^{40, 41}\) Thus use of our suggested LVEF cutpoints would tend to include a slightly larger percentage of patients with acute myocardial infarction in the high-risk group if patients were screened by radionuclide techniques. Ideally, radionuclide images would be obtained using isotopes with very short half-lives to minimize the risk of radiation exposure to medical staff should further invasive procedures be necessary. Echocardiography can also assess left ventricular function, but LVEF determined with this method correlates poorly with contrast angiographic LVEF, especially when regional asynergy is present.\(^{42, 43}\) Nonetheless, regional left ventricular wall motion can be assessed accurately in most patients by this method.\(^{43, 44}\) The appropriate correlations between our contrast angiographic LVEF cutpoints and echocardiographically defined regional wall motion abnormalities need to be determined.

Significant implications for the management of patients during the early hours of acute myocardial infarction can be derived from analysis of the survival curves in figures 3 and 4. Intracoronary streptokinase treatment improves prognosis for survival in all treated patients. However, in patients who are at low risk for death in the first place, both the potential for improved survival and the magnitude of improved probability of survival with streptokinase treatment are quite small. Intravenous thrombolytic agents, such as tissue-type plasminogen activator, that have a low risk of complication could still be justified in this low-risk group. However, determination of LVEF and location of the infarct by noninvasive testing at the time of hospitalization should be able to save the substantial number of patients that would fall in this group the risks (and the costs) of invasive procedures that would have little potential for significantly altering mortality. For patients in the high-risk group, on the other hand, these models demonstrate a dramatic improvement in probability of 1 year survival with achievement of complete reperfusion. For high-risk patients, the potential benefit of achieving complete reperfusion may significantly outweigh the potential risks (and costs) of invasive interventional therapies. Emergent coronary angiography to document reperfusion status with treatment is particularly indicated in this group. Emergent percutaneous transluminal coronary angioplasty or emergent coronary bypass surgery might be of particular benefit if thrombolytic therapy fails to yield complete reperfusion in these patients.

Finally, this analysis has significant implications for the design of trials of interventional therapy in patients with acute myocardial infarction. If mortality is the end point to be evaluated, adequate numbers of high-risk patients must be enrolled and the randomization process must evenly divide the high-risk patients among the different treatment groups. The methods outlined here provide a means for testing these conditions. By limiting selection of patients for such trials to those at high risk for 1 year mortality, the size of these trials could be reduced while still providing an adequate test of the therapy being evaluated.

In summary, our analysis of the relationships between factors identified in the first hours of acute myo-
cardiac infarction and 1 year survival has yielded two important findings. First, LVEF determined in the early hours of acute myocardial infarction is the most important predictor of subsequent 1 year outcome. Second, mathematical models developed here identify high- and low-risk patient groups based on factors defined in the first hours of acute myocardial infarction and illustrate the impact of interventional therapies given 3.5 to 6.0 hr after onset of the event.

The thoughtful reviews of the manuscript and suggestions by Drs. Harold Dodge and Florence Sheehan were appreciated. We are grateful to Sylvia Duncan for manuscript preparation.

Appendix 1: Model for determination of probability for 1 year survival

\[
P = (1 + e^{\beta_1 \cdot \text{EF} + \beta_2 \cdot \text{LVEF}})^{-1}
\]

\[
x = 4.099 + (-0.123 \cdot \text{EF}) + (-1.401 \cdot \text{infarct location}) + (-1.126 \cdot \text{streptokinase therapy})
\]

EF: Expressed as a whole number

Infarct location:
- 0 = anterior by ECG (LAD by angiography)
- 1 = inferior by ECG (RCA or CIRC by angiography)

Streptokinase treatment:
- 0 = no streptokinase infusion
- 1 = streptokinase infusion

Appendix 2: Model for determination of probability of 1 year survival including reperfusion status

\[
P = (1 + e^{\beta_1 \cdot \text{EF} + \beta_2 \cdot \text{LVEF}})^{-1}
\]

\[
x = 3.355 + (-0.094 \cdot \text{EF}) + (-2.343 \cdot \text{infarct location}) + (-2.417 \cdot \text{reperfusion status})
\]

EF: Expressed as a whole number

Infarct location:
- 0 = anterior by ECG (LAD by angiography)
- 1 = inferior by ECG (RCA or CIRC by angiography)

Reperfusion status:
- 0 = no reperfusion or partial reperfusion after intracoronary streptokinase
- 1 = complete reperfusion after streptokinase

Western Washington Intracoronary Streptokinase Trial


Italics denote physicians who are administratively responsible for the trial at their institutions.

References


Risk stratification for 1 year survival based on characteristics identified in the early hours of acute myocardial infarction. The Western Washington Intracoronary Streptokinase Trial.
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