Identification of Acute Myocardial Infarction Patients Suitable for Early Hospital Discharge After Aggressive Interventional Therapy

Results From the Thrombolysis and Angioplasty in Acute Myocardial Infarction Registry

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Background. Very early (day 4) hospital discharge has recently been proposed for selected patients with acute myocardial infarction (MI). The purpose of this study was to determine the most useful factors for identifying acute MI patients treated with aggressive interventional therapy who could be safely discharged on day 4.

Methods and Results. We studied 708 patients enrolled in the Thrombolysis and Angioplasty in Acute Myocardial Infarction trials I–III. Patients dying in the first 3 days and those with early (days 1–3) emergency coronary artery bypass graft surgery (CABG), late elective CABG (≥ day 4), or urgent/emergency CABG resulting from a late elective coronary angioplasty were excluded. The remaining 580 patients were randomly divided into a training sample (group 1) that was used to build a logistic regression model for predicting the absence of a late major complication and a test sample (group 2) that was used to validate this model. For this study, patients were considered appropriate for day 4 hospital discharge if they did not experience any of the following for 30 days after MI: death, reinfarction, cardiogenic shock, pulmonary edema, sustained hypotension, sustained ventricular tachycardia, high-grade atrioventricular block, acute ventricular septal defect, and recurrent ischemia necessitating urgent CABG. In group 1, four variables were independent predictors of freedom from late major complications: absence of early sustained ventricular tachycardia or ventricular fibrillation, absence of early sustained hypotension or cardiogenic shock, fewer coronary arteries with significant (≥75%) stenosis, and a higher left ventricular ejection fraction. In group 2, 23% of patients had a logistic model prediction of a 3% or less chance of a late complication. These patients had no deaths or reinfarctions by day 30 and a 3% late major complication rate.

Conclusions. The results of early cardiac catheterization and the absence of selected early (days 1–3) major complications allow identification of a low risk subgroup of acute MI patients that may be suitable for very early discharge. (Circulation 1991;83:1186–1193)

Over the past several decades, the approach to the rehabilitation of the patient with acute myocardial infarction (MI) has undergone considerable evolution. Prolonged forced bed rest in the 1940s was replaced by “armchair treatment” in the 1950s, and extended hospitalizations were superseded in the 1970s by “early discharge” 7–10 days after admission.

Recently, the treatment of acute MI has changed dramatically with the advent of thrombolytic therapy and the increased use of interventional catheterization procedures early after the onset of symptoms. There is now considerable evidence that the in-hospital and long-term prognosis of an MI treated...
with aggressive interventional therapy is significantly improved over that observed with conservative treatment.2-4 One issue this raises is whether the successful use of such therapy has any implications for the duration of hospitalization. Topol and colleagues5 at the University of Michigan have shown, in a randomized controlled trial, that hospital discharge after 3 days is feasible in carefully selected patients with an uncomplicated MI and may reduce health care costs. It remains uncertain, however, whether the optimal criteria for selecting patients for such very early discharge in the thrombolytic era are the same as those identified previously for conservatively treated patients.1 It is also uncertain whether aggressive interventional procedures such as acute-phase percutaneous transluminal coronary angioplasty (PTCA) affect the feasibility or safety of very early discharge.

This study had two goals: 1) to examine a large group of carefully studied patients with acute MI treated with aggressive interventional protocols in the Thrombolysis and Angioplasty in Acute Myocardial Infarction (TAMI) trials I-III to identify the best early predictors of low risk status between day 3 and day 30 after MI and 2) to evaluate the safety of an algorithm for very early discharge based on these predictors.

### Methods

#### Study Population

Patients enrolled in TAMI trials I-III were considered for inclusion in this study. Enrollment and exclusion criteria in the TAMI trials have remained consistent and have been published in detail previously.6-8 Briefly, patients were eligible for inclusion in TAMI I-III if the following entry criteria were met: 1) ischemic symptoms lasting for more than 20 minutes and for up to 6 hours, 2) accompanying ST elevation of 1 mm or more in two or more contiguous leads, 3) no contraindication to thrombolytic therapy, 4) age less than 76 years, 5) no cardiogenic shock on presentation, and 6) no prior coronary artery bypass graft surgery (CABG). A total of 708 patients met these criteria and were enrolled in the first three TAMI trials.

Patients clearly ineligible for a day 4 early discharge strategy were excluded from further analysis: 22 patients who died and 40 patients who had CABG during the first 3 days of hospitalization. In addition, patients whose clinical course was altered by an elective CABG after day 3 (n=61) or an elective PTCA after day 3 with resulting ischemic complications necessitating urgent or emergency CABG (n=5) were eliminated from the analysis. Thus, the final study population comprised 580 patients (Figure 1).

#### The TAMI Trials

The TAMI I study was designed to examine the role of acute PTCA after administration of thrombolytic therapy.6 High dose (150 mg) intravenous tissue-type plasminogen activator (t-PA) was given to 386 patients for 6–8 hours. All patients had coronary angiography at 90 minutes after drug administration. Patients with infarct artery reperfusion and a residual subtotal stenosis that was felt to be suitable for PTCA (n=197) were randomized to immediate or deferred PTCA. Patients with a persistently occluded infarct artery (n=96) underwent a “rescue” PTCA. The remaining 39 patients had either severe coronary artery disease not amenable to PTCA or minimal lesion syndrome.

TAMI II was a pilot study in 147 patients; synergy between t-PA and urokinase was studied.7 Five different dose combinations of t-PA (25 mg or 1.0 mg/kg) and urokinase (0.5–2.0 million units) given over 1 hour were tested. All patients underwent an acute cardiac catheterization; the primary end point of the study was infarct vessel patency at 90 minutes.

In TAMI III, 175 patients were randomized to received either 100 mg t-PA alone or 100 mg t-PA plus a 10,000-unit heparin bolus.8 The t-PA was given over 1 hour, and all patients underwent a 90-minute angiogram. The primary end point of the study was infarct vessel patency at 90 minutes.

#### Cardiac Catheterization and Coronary Angioplasty

After initiation of thrombolytic therapy, patients in all three trials were transferred to the cardiac catheterization laboratory where coronary angiography
was performed with visualization of the infarct vessel at 90 minutes, as described previously.6–8 In all three trials, patients with an occluded infarct vessel (Thrombolysis in Myocardial Infarction [TIMI] flow pattern grade 0 or 1) and suitable coronary anatomy (absence of significant left main or very distal disease) at 90 minutes underwent a rescue PTCA procedure, whereas patients with patent infarct-related arteries that were not suitable for PTCA were treated with medical therapy or CABG as indicated.

In TAMI I, suitable patients with a patent infarct artery at 90 minutes were randomized to early or delayed PTCA. In TAMI II and III, early PTCA was only performed for thrombolytic failure (TIMI grade 0–1) or reduced coronary flow (TIMI grade 2) with objective electrocardiographic (i.e., ST segment shifts) or hemodynamic (i.e., pulmonary edema or sustained hypotension) signs of ongoing ischemia. The details of the catheterization and PTCA procedures used in these trials have been published previously.6–8

Data Collection and Definitions

Multiple data items were collected prospectively by study nurses throughout the patients' hospital course. The presence or absence of major complications was noted on a daily basis until hospital discharge. During the first three TAMI studies, there were only minor modifications made in the data items collected, making it possible to pool these three data sets for the current analysis. Follow-up procedures have been described previously. Major complications were as follows: death during the first 30 days after study enrollment, reinfarction in the first 30 days after study enrollment, cardiogenic shock, pulmonary edema, sustained (>1-hour) hypotension, sustained (>30-second) ventricular tachycardia, ventricular fibrillation, second- or third-degree atrioventricular block, acute ventricular septal defect, and recurrent ischemia necessitating emergency or urgent CABG. Minor complications included the following: definite angina (symptoms plus ST-T changes), severe sinus bradycardia (<40 beats/min), atrial arrhythmias, non-sustained (<30-second) ventricular tachycardia, and congestive heart failure (by exam or chest x-ray). “Early” complications occurred during the first 3 days of hospitalization; “late” major complications were those occurring after the third day of hospitalization.

Data Analysis

Descriptive statistics were generated using percentages for discrete variables and medians and quartile ranges (25th and 75th percentiles) for continuous variables. For the study analyses, the patient population was randomly divided into two equal-sized groups. Group 1, the training sample, was used to discover the best combination of clinical characteristics and early (days 1–3) complications for predicting an uncomplicated course from day 4 to day 30. This combination of factors was then tested in the remaining independent sample of patients (group 2) to discover how well the predictive rule performed in identifying a low-risk group potentially suitable for very early (day 4) hospital discharge. Stepwise logistic regression analysis was used to discover the best combination of variables for selecting very early discharge candidates. The accuracy of the resulting predictive model was assessed by comparing predictions in the training and test samples to assess the reproducibility of risk stratification and by calculating the area under the receiver operating characteristic (ROC) curve for the model predictions in these two samples.9,10 In the logistic regression analyses, continuous variables (e.g., age and ejection fraction) were analyzed in their original continuous form; variables such as number of diseased vessels and TIMI grade were analyzed as ordinal variables.

Results

Study Population

The baseline characteristics of the 580 study patients are shown in Table 1. Overall, 80% of the patients were men, and the median age was 55 years. Forty percent of patients had an anterior MI. Seventy percent of patients had an open infarct vessel (TIMI grade 2 or 3) on the 90-minute angiogram. Multivessel coronary disease was present in 39%, and the median ejection fraction was 0.53. Overall, 45% of patients underwent an acute-phase PTCA as part of the initial catheterization procedure.

### Table 1. Baseline Clinical and Catheterization Characteristics of Total Study Population

<table>
<thead>
<tr>
<th>Variable</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>80%</td>
</tr>
<tr>
<td>Age</td>
<td>55 (48–63)*</td>
</tr>
<tr>
<td>History of prior angina</td>
<td>51%</td>
</tr>
<tr>
<td>Anterior MI</td>
<td>40%</td>
</tr>
<tr>
<td>Number of diseased vessels</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>8%</td>
</tr>
<tr>
<td>1</td>
<td>53%</td>
</tr>
<tr>
<td>2</td>
<td>28%</td>
</tr>
<tr>
<td>3</td>
<td>10%</td>
</tr>
<tr>
<td>Left main</td>
<td>1%</td>
</tr>
<tr>
<td>TIMI grade at 90 minutes</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>23%</td>
</tr>
<tr>
<td>1</td>
<td>7%</td>
</tr>
<tr>
<td>2</td>
<td>17%</td>
</tr>
<tr>
<td>3</td>
<td>53%</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>0.53 (0.44–0.60)*</td>
</tr>
<tr>
<td>Acute PTCA</td>
<td>45%</td>
</tr>
<tr>
<td>Representation in study population</td>
<td></td>
</tr>
<tr>
<td>TAMI I</td>
<td>52%</td>
</tr>
<tr>
<td>TAMI II</td>
<td>23%</td>
</tr>
<tr>
<td>TAMI III</td>
<td>26%</td>
</tr>
</tbody>
</table>

MI, myocardial infarction; TIMI, Thrombolysis in Myocardial Infarction trial; PTCA, percutaneous transluminal coronary angioplasty; TAMI, Thrombolysis and Angioplasty in Myocardial Infarction trial; n=580 patients in total study population.

*Continuous variables are displayed as median (25th–75th percentile).
TABLE 2. Early (Days 1–3) Complications in Total Study Population

<table>
<thead>
<tr>
<th>Variable</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major complications</td>
<td></td>
</tr>
<tr>
<td>Shock</td>
<td>1%</td>
</tr>
<tr>
<td>New pulmonary edema</td>
<td>10%</td>
</tr>
<tr>
<td>Sustained VT</td>
<td>13%</td>
</tr>
<tr>
<td>VF</td>
<td>11%</td>
</tr>
<tr>
<td>Sustained hypotension</td>
<td>14%</td>
</tr>
<tr>
<td>Advanced AV block</td>
<td>12%</td>
</tr>
<tr>
<td>Reinfarction</td>
<td>5%</td>
</tr>
<tr>
<td>Any of the above</td>
<td>42%</td>
</tr>
<tr>
<td>Two or more of the above</td>
<td>17%</td>
</tr>
<tr>
<td>Minor complications</td>
<td></td>
</tr>
<tr>
<td>Definite angina</td>
<td>12%</td>
</tr>
<tr>
<td>Severe sinus bradycardia</td>
<td>23%</td>
</tr>
<tr>
<td>Atrial arrhythmias</td>
<td>6%</td>
</tr>
<tr>
<td>Nonsustained VT</td>
<td>37%</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>17%</td>
</tr>
<tr>
<td>Any of the above</td>
<td>64%</td>
</tr>
</tbody>
</table>

VT, ventricular tachycardia; VF, ventricular fibrillation; AV, atrioventricular; n=580 patients in total study population.

As shown in Table 2, 42% of the study population had a major complication during the first 3 hospital days, including cardiogenic shock in 1%, new-onset pulmonary edema in 10%, sustained (≥1-hour) hypotension in 14%, and reinfarction in 5%. Minor complications were also prevalent, including definite angina in 12% and evidence of congestive heart failure in 17%.

Logistic Model Derivation and Validation

After randomly dividing the patients into two equal-sized groups (group 1, n=289; group 2, n=291), there was no significant difference in the distribution of the characteristics shown in Tables 1 and 2. In the training sample (group 1), 38 patients (13%) had a late major complication (day 4 or later). Using stepwise logistic regression analysis, four variables were found to be independent predictors of late major complications (Table 3): sustained ventricular tachycardia or ventricular fibrillation (days 1–3), sustained hypotension or cardiogenic shock (days 1–3), a depressed ejection fraction at baseline, and more coronary arteries with significant stenosis (≥75%) on the baseline angiogram. The area under the ROC curve for this four-variable model in the training sample was 0.802; in the test sample, the area under the ROC curve was 0.742. When the patients who were excluded because of elective CABG or elective PTCA followed by urgent/emergency CABG (see Figure 1) were added back to the test sample (group 2), the area under the ROC curve for the model was 0.723. In addition, there was no evidence of a lack of fit of the model's component variables (χ²=1.3, 3 degrees of freedom) in group 2 with these patients included.

TABLE 3. Prediction of Late Complications by Logistic Regression Analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariable</th>
<th>Multivariable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sustained VT or VF</td>
<td>14</td>
<td>10</td>
</tr>
<tr>
<td>Sustained hypotension or shock</td>
<td>13</td>
<td>9</td>
</tr>
<tr>
<td>Number of diseased vessels</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>Ejection fraction at baseline</td>
<td>12</td>
<td>5</td>
</tr>
<tr>
<td>New pulmonary edema</td>
<td>13</td>
<td>...</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>12</td>
<td>...</td>
</tr>
<tr>
<td>Anterior MI</td>
<td>8</td>
<td>...</td>
</tr>
<tr>
<td>Age</td>
<td>4</td>
<td>...</td>
</tr>
</tbody>
</table>

VT, ventricular tachycardia; VF, ventricular fibrillation; MI, myocardial infarction.

Other variables tested were not significant in univariable analysis: sex, Thrombolysis in Myocardial Infarction trial grade at 90 minutes, acute coronary angioplasty, which Thrombolysis and Angioplasty in Myocardial Infarction trial patient was enrolled in, history of prior angina, definite angina (days 1–3 after hospitalization), severe sinus bradycardia (days 1–3), atrial tachyarrhythmias (days 1–3), advanced atrioventricular block (days 1–3), nonsustained VT (days 1–3), and reinfarction (days 1–3).

Risk Score Derivation and Validation

For illustrative purposes, a late complication risk score was formed that arbitrarily assigned one point each for early sustained ventricular tachycardia or ventricular fibrillation, early sustained hypotension or cardiogenic shock, multivessel coronary artery disease, and an ejection fraction less than 40%. Thus, a score of 0 indicated the lowest risk group, and 4 indicated the highest risk of late complications. Patients in whom a valid baseline ejection fraction could not be calculated (30 patients in group 1 and 37 patients in group 2) were excluded from these calculations. Because of the small numbers of patients with high scores, a composite high-risk score (2–4) was formed.

Table 4 shows the observed rate of late complications for each level of the risk score in the training sample (group 1) and the test sample (group 2). The risk stratification provided by the score in the new sample (group 2) was very close to what had been observed in the derivation sample (group 1), indicat-

TABLE 4. Rate of Late Complications

<table>
<thead>
<tr>
<th>Score</th>
<th>Training sample</th>
<th>Test sample</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Validation of late complication risk score*</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>4/106 (4%)</td>
<td>6/105 (6%)</td>
</tr>
<tr>
<td>1</td>
<td>13/104 (13%)</td>
<td>10/93 (11%)</td>
</tr>
<tr>
<td>≥2</td>
<td>15/49 (31%)</td>
<td>14/56 (25%)</td>
</tr>
<tr>
<td></td>
<td>Death and reinfarction rates at 30 days after MI</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1/106 (1%)</td>
<td>0/105 (0%)</td>
</tr>
<tr>
<td>1</td>
<td>2/104 (2%)</td>
<td>4/93 (4%)</td>
</tr>
<tr>
<td>≥2</td>
<td>3/49 (6%)</td>
<td>5/56 (9%)</td>
</tr>
</tbody>
</table>

*Sample numbers represent number of patients with a late major complication at 30 days after myocardial infarction (MI) divided by total number of patients in risk group for training sample (group 1) and test sample (group 2). Percentage of late complication observed in each risk stratum is shown in parentheses.
ing that the score provided reproducible stratification for the entire risk spectrum (low to high). In the total population, 30% of patients (211 of 708) were identified as low risk. In group 2, the six late complications observed in the low risk group were as follows: 2–3° atrioventricular block (three patients), new pulmonary edema (one patient), and urgent/emergency CABG for recurrent ischemia (two patients). There were no deaths or reinfarctions in this low risk group by day 30 (Table 4). These results were unchanged when the patients with elective CABG between day 4 and day 30 or elective PTCA followed by urgent/emergency CABG (see Figure 1) were included in the study population; in the test sample, 6 of 109 patients with a score of 0 had a late major complication (6%), and 1 of 109 (1%) had death or reinfarction by day 30. We also evaluated whether the study results were affected when we excluded the patients treated with acute PTCA (45% of the study population, Table 1) or the nine patients in the TAM1 I–III trials who ended up with a final diagnosis other than acute MI. In neither case was the performance of our early discharge model or risk score significantly affected.

The 4–6% prevalence of late complications in the low risk groups of both samples (Table 4) may reflect, in part, the failure of the illustrative risk score to properly weight the four component variables. Thus, when the full logistic model (from which the risk score was derived) was tested in the group 2 patients and when low risk was defined as a model prediction of a 0–3% chance of a late complication, we identified 58 patients (23%) as low risk. This group had a 3% prevalence of late complications and a 0% prevalence of death or reinfarction by day 30. The two late complications observed in this low risk group were 2–3° atrioventricular block (one patient) and urgent/emergency CABG for recurrent ischemia (one patient). An even stricter definition of low risk (model prediction of a 0–2% chance of late complications) yielded a smaller group (27 patients, or 11% of test sample) with no late complications.

Discussion

The most important finding of this study is that 30% or more of acute MI patients treated with aggressive interventional therapy are at very low risk of major complications between 4 and 30 days after their infarct and may be suitable for very early (day 4) hospital discharge. This study is the first to use multivariable analysis to identify the best predictors of safe very early discharge in acute MI patients treated with aggressive reperfusion therapy. This study is also one of the first to construct an early discharge algorithm in acute MI patients and to validate that algorithm in an independent sample of patients.

The impetus to identify patients suitable for very early discharge after an acute MI stems from a desire to minimize unnecessary use of medical resources and to maximize the rehabilitation of the patient.11 Shortening the hospital stay offers the potential for accomplishing both of these goals, assuming that patients discharged on day 4 are not harmed by the occurrence of serious postdischarge complications that would be treated more promptly and successfully were the patient still in the hospital.1,12

One of the major issues that must be confronted in any proposal for very early discharge after acute MI is how low the risk must be to make the strategy an acceptable medical practice. There is currently no consensus on this topic, which has received relatively little discussion in the medical literature. In the absence of a consensus, clinicians have two major options. First, low risk can be defined as the current average risk for an uncomplicated MI patient in the month following a standard 7–10-day hospital stay. This risk of posthospital events is tacitly accepted by the medical profession and by patients as reasonable. Second, a higher risk of events can be accepted because of an associated significant reduction in medical care costs. We feel that, at present, the former criterion is most appropriate with the caveat that accepting a higher risk of postdischarge complications may ultimately be found to be more cost-effective from a health policy perspective.

McNeer and colleagues10 in 1978 demonstrated that a screening algorithm to detect uncomplicated MI patients on the fifth hospital day identified 67 of 158 consecutive patients (42%) as low risk. Half of these patients were discharged at 1 week; the remainder had an average hospital stay of 11±2 days. At 3 weeks from the date of infarction, neither group had any deaths, nonfatal MIs, or cardiac rehospitalizations. Because of the small sample size of this study, these observations are consistent with up to a 4% postdischarge complication rate (upper 95% confidence limit).

In a follow-up community hospital validation of the McNeer algorithm,11 81 of 245 consecutive acute MIs (33%) were identified as uncomplicated by day 5,13 in this group, 3 patients (4%) had recurrent nonfatal MI within the first 30 days. Other investigators have obtained similar results in conservatively treated patient populations. Thus, Madsen et al14 developed a Cox regression model for predicting risk of death in 259 acute MI patients based on events occurring during the first 5 hospital days. Using this model, 134 patients (52%) were designated as low risk (≤5% predicted chance of death). In this group, there were one cardiac arrest and five reinfarctions (two of which were fatal) between day 6 and day 30, for an overall major complication rate of 4%. Using a more conservative definition of low risk (≤2% risk of death), a smaller cohort eligible for early discharge was identified, but the patients with postdischarge reinfarction were eliminated. A more sophisticated approach by Madsen and colleagues12 using death, cardiac arrest, or cardiogenic shock as end points identified 67% of their MI patients, who were discharged between day 6 and day 15, with a predicted risk of 2% or less. There were two unexpected deaths
between hospital discharge and day 30 (a 2% event rate). In a recent randomized trial of day 4 early discharge in acute MI patients treated with aggressive interventional therapy, Topol and colleagues\(^\text{9}\) observed no deaths and two reinfarctions between day 4 and day 30 in 80 patients (event rate of 3%) identified as eligible for this strategy.

One difficulty in assessing acceptable cardiac event rates after hospital discharge is inconsistency in the literature in what is counted as a "cardiac event." Our approach was to include any major event that might conceivably receive better treatment if the patient were still hospitalized. This has the advantage of trying to ensure that very early discharge is considered only for the truly lowest risk patients. The assumption that these events would all be better treated in a hospital, however, may not be correct. Patients with recurrent ischemia, for example, even if it is severe, may suffer no permanent harm if medical treatment is delayed by the time necessary to mobilize an emergency squad and bring the patient from home to the nearest emergency room. Furthermore, many hospitals do not have the capacity to monitor uncomplicated post-MI patients electrocardiographically for more than 2 or 3 days. An unmonitored post-MI patient may, therefore, suffer an unobserved cardiac arrest in a hospital and not be resuscitated in the critical first 5 minutes. Previous investigators of early post-MI discharge have defined a cardiac event as death alone,\(^\text{14}\) death or reinfarction, death or reinfarction or new angina,\(^\text{11}\) or death, shock, or cardiac arrest.\(^\text{12}\)

Based on these older reports of what is now standard practice, a postdischarge hard cardiac event rate (death or reinfarction) of between 2% and 5% within the first 30 days would be consistent with current medical practice.\(^\text{15}\) Using our very early discharge risk score allowed us to identify 41% of our validation patient population (group 2) with an observed 30-day death or reinfarction rate of 0% and a 30-day major complication rate of 6%, which would clearly fall within the available boundaries of currently acceptable practice. Use of the parent logistic model and a more stringent definition of low risk allowed us to identify smaller subgroups of group 2 with rates of 3% or less of any major complication while preserving the 0% rate of death and reinfarction.

Early discharge strategies in the prethrombolytic era have largely been based on empirical selection of criteria to define low risk. This has resulted in a variety of risk stratification strategies.\(^\text{1}\) When multivariable statistical methods have been applied to this problem, only a handful of the numerous stratifying variables proposed for the empirical classification schemes have been found to provide independent prognostic information.\(^\text{12}\) This may be because only a few of these variables are actually necessary to identify low risk patients who are suitable for early discharge. Alternatively, these multivariable studies may not have included enough patients with enough outcome events to allow the important predictors to be identified.

The variables selected in this study for identification of very early discharge candidates are consistent with previous conceptual outlines of risk stratification in postinfarction patients.\(^\text{16–20}\) Thus, our analysis indicates that the amount of dysfunctional myocardium (as judged by the ejection fraction and the development of early sustained hypotension not due to volume depletion), the amount of jeopardized myocardium and the potential for recurrent coronary events (as reflected by the number of diseased vessels), and the amount of electrical instability (assessed by the development of early sustained ventricular tachycardia or ventricular fibrillation) each independently contribute to the identification of patients at increased risk of major cardiac events by day 30. A number of other variables were probably not selected in this analysis because they provided redundant and less accurate prognostic information in our population. For example, the electrocardiographic infarct location may not provide unique prognostic data once left ventricular performance has been measured,\(^\text{19,21}\) and the prognostic information provided by post-MI angina may also be captured by the severity of the patient's coronary artery disease.\(^\text{22}\) Pulmonary edema (days 1–3) and congestive heart failure (days 1–3) were significant in univariate analysis (Table 3) but did not add independent predictive information to the final model, probably because of the inclusion in the model of other descriptors of myocardial dysfunction.

Some of the variables that were not selected in our analysis are worthy of comment. Age intuitively seems like an appropriate risk stratification variable, and older patients with acute MI have been shown in the past to have a higher hospital mortality rate,\(^\text{23}\) even with aggressive interventional therapy.\(^\text{3,4,24,25}\) In this analysis, the age of the study patients was restricted to 75 years or less by the TAMI entry criteria, and the median age was 55, which suggests that there may not have been enough patients over age 70 to detect an independent effect of age. Part of the prognostic importance of age may also have been explained by other variables selected in the analysis, such as number of diseased vessels and ejection fraction. Similarly, female sex has been identified previously as a risk factor for hospital mortality after MI\(^\text{26}\) but was not selected in our analysis. As with age, part of the prognostic importance of female sex can be described with other variables.\(^\text{26}\) In addition, since women made up only 20% of the study population, the power in this study for detecting a small independent effect on cardiac event rates was limited.

Many postinfarction risk stratification strategies involve the use of a predischarge functional test, such as a treadmill or an exercise radionuclide study.\(^\text{27,28}\) Such data were not available in the present study, and it is possible that an even more powerful method of identifying very low risk patients for day 4 discharge could be attained by including functional test
information. On the other hand, the added value of functional testing in post-MI patients whose coronary anatomy and left ventricular function are already known (as in the present study) may be substantially less than in the traditional conservatively treated patient population.

Since the advent of thrombolytic therapy and aggressive interventional therapy for acute MI, only one group has explored the implications of these therapies for more aggressive early discharge. Topol and colleagues have shown that early (day 4) exercise testing can be done in MI patients treated with acute interventional therapy with no apparent adverse consequences for left ventricular remodeling or subsequent prognosis. In a small randomized trial, Topol et al demonstrated the feasibility and potential cost savings of day 4 discharge. Although the current study arrived at a low risk population with only a subset of the variables used by Topol et al, our results do support the proposal that some aggressively treated acute MI patients can be discharged as early as day 4 with an acceptable 30-day mortality and major complication rate.

One issue that must be explored further is whether a day 4 post-MI discharge strategy that requires acute or early cardiac catheterization can provide medical and quality-of-life benefits that are equivalent to or better than those currently being obtained with more traditional management strategies, at an equivalent or reduced cost. Ross and colleagues have validated an algorithm in conservatively treated acute MI patients that allows a low risk group to be identified while avoiding angiography in approximately half of their population. In the short term (i.e., considering only the initial MI hospitalization), the costs of an early cardiac catheterization may not be recovered by reducing the length of stay by 3–4 ward days in most hospitals. If early cardiac catheterization allows clinicians to forgo predischARGE functional testing or to shift from an expensive test (such as an exercise nuclear study) to an inexpensive one (such as a treadmill test), the very early discharge strategy may approach a cost-neutral or cost-saving position.

The long-term cost-effectiveness implications of very early discharge are more complex and difficult to measure. For example, early catheterization may save lives by identifying the highest risk patients for triage to revascularization but may also result in revascularization being done in patients who would have done equally well or better with more conservative management. Since revascularization is now recognized as a palliative rather than a curative procedure, premature revascularization may set in motion a series of events that, from a cost-effectiveness point of view, would take a decade or more to be manifest.

The psychosocial effects of very early discharge also need to be evaluated carefully. In the trial by Topol and colleagues, psychological testing of the patients and their spouses showed generally favorable trends over the first month in the very early discharge group. There was also a trend toward an earlier return to work in this group.

There are several notable limitations to this study. First, the TAMI trials were not designed to examine the issue of early discharge. In fact, the design of these trials specifically precluded discharge before day 7 by requiring a 1-week follow-up catheterization study to evaluate coronary patency and left ventricular function. Enrollment criteria and data collection methods for the TAMI I–III trials were similar enough to permit pooling of these separate trials for this analysis, and there was no evidence that the specific study in which a patient was enrolled affected the patient’s suitability for very early discharge (Table 3). However, it is possible that temporal trends in these three sequential MI trials could have affected the results of our analysis. Furthermore, patients eligible for acute MI trials such as the TAMI studies represent a low risk subset of the total acute MI population.

The performance of our early discharge algorithm in a less selected acute MI cohort thus remains to be determined. Second, some uncomplicated patients had a late PTCA procedure for prognostic reasons, and their outcome with a more conservative approach is thus unknown. Use of PTCA at varying points in the recovery phase of an acute MI reflects current clinical practice. We found no evidence that acute PTCA affected our results, but our model’s risk stratification might be altered in other acute MI populations with different patterns of PTCA use. Third, we excluded patients with a late elective CABG (n=61) or a late elective PTCA complicated by the need for urgent/emergency CABG (n=5) (Figure 1), and these exclusions could have biased our assessment of the performance of our very early discharge algorithm. However, when we repeated our analyses with these patients included, the results were unchanged. A formal test using the logistic regression model revealed no evidence of lack of fit of our four-variable model (χ²=1.3, 3 degrees of freedom) in the validation sample (group 2). In addition, the risk stratification shown in Table 4 was unchanged by inclusion of these patients. Thus, exclusion of these patients had no discernible effects on the results of the study. Fourth, our early discharge algorithm is based, in part, on early catheterization data, and in many practice settings, these data will not be available. Finally, our patient population, which is one of the largest used to date to study early discharge, may still be too small to accurately account for rare late complications.

In summary, this study shows that in an acute MI population the results of early cardiac catheterization and the absence of selected early (days 1–3) major complications identified a subgroup of very low risk patients comprising 15–30% of the total group. This low risk subgroup had no deaths or reinfarctions by day 30 and had a very low rate of other major complications. Such patients may be suitable for very early (day 4) discharge. This study should provide
useful guidance in designing future trials of very early discharge after acute MI.

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