Thrombolytic Therapy for Acute Myocardial Infarction*

Eric R. Bates, M.D.; and Eric J. Topol, M.D.

Thrombolytic therapy in AMI restores infarct artery patency, preserves LV function, and decreases hospital mortality. Although hemorrhagic complications including stroke can occur, the incidence of stroke is not increased compared with control groups. Aspirin must be administered as soon as possible to inhibit platelet function, and an adjunctive role for early β-blocker therapy may be important. Acute cardiac catheterization and coronary angioplasty need not be routinely performed in stable patients after tPA therapy, but should be considered in unstable patients. Two trials suggest that aggressive use of coronary angioplasty or bypass graft surgery before hospital discharge to preserve infarct artery patency and to prevent postinfarction ischemia is associated with an important improvement in long-term prognosis. Thrombolytic therapy should be considered standard care for patients whose ischemic chest pain lasts 20 min to at least 6 h in duration and who have an injury current on their ECG unless they are at increased risk for bleeding. The need for and timing of cardiac catheterization, coronary angioplasty, and surgical revascularization after AMI requires further evaluation.

Ischemic heart disease is the leading cause of mortality in industrialized societies. Mortality is usually caused by either ventricular tachyarrhythmias or heart failure following acute or remote MI. Whereas antiarrhythmic drug therapy and electrical defibrillation have been clinically available for years to treat the electrical complications of MI, only recently in the form of thrombolytic therapy has there been an effective means for preserving LV function and further decreasing in-hospital mortality from MI.

CORONARY THROMBOSIS AND THROMBOLYTIC THERAPY

Herrick first postulated in 1912 that coronary thrombosis initiated AMI. This concept was debated for decades; however, because pathologic studies failed to demonstrate coronary thrombosis in variable numbers of patients with severe coronary disease who died of AMI. An angiographic and surgery study by DeWood et al conclusively resolved the controversy by demonstrating the presence of thrombosis in 87% of patients studied within 4 h of symptom onset. Thrombosis was seen in only 65% of patients studied 12–24 h after symptom onset because of spontaneous thrombolysis, explaining the inability of the previous autopsy studies to detect thrombus. This landmark study established a pathophysiologic basis for thrombolytic therapy and ushered in the modern thrombolytic era.

Thrombolytic therapy for AMI was not a new concept when DeWood et al performed their study. Intravenous streptokinase was initially used in the late 1950s for this purpose and was tested in several multicenter trials in the 1960s and 1970s. Unfortunately, improvement in LV function and mortality were found inconsistently because of low patency rates and inadequate salvage of ischemic muscle due to late implementation of therapy, inadequate doses, and use of the IV route for drug delivery. Immediate arteriographic recanalization following intracoronary injection of streptokinase during AMI was first reported by Chazov et al and later by Rentrop et al. Other trials quickly established that reperfusion rates of approximately 75% could be achieved with this therapy, leading to approval by the FDA of both streptokinase and urokinase for intracoronary use in AMI. Intravenous streptokinase and tPA were also approved in November 1987 for clinical use following proof that LV function was improved and mortality decreased when therapy was instituted early after symptom onset. Intravenous urokinase and anisoylated plasminogen streptokinase activator complex (APSAC) are two other potentially useful agents that may be approved for use within the year.

REPERFUSION AND HOSPITAL OUTCOME

Reimer et al demonstrated in dog studies that myocardial necrosis following acute arterial occlusion occurs over several hours (Fig 1). Myocytes in the subendocardium are irreversibly injured first, with a wavefront of cell death moving progressively toward the subepicardium. The amount of ischemic muscle at risk for necrosis that becomes irreversibly injured is therefore dependent on the duration of arterial occlusion; conversely, myocardial salvage is dependent on time to reperfusion. Clinical thrombolytic studies have confirmed the concept that “time is muscle.” Enzymatically determined infarct size was directly related to time to treatment in the Netherlands Trial. The impact of time to treatment on mortality was dramatically demonstrated in the GISSI trial, where in-hospital mortality was decreased by 47%, 23%, and 17% in patients treated within 1 h, 3 h, and 3–6 h, respectively. Since all of the other recent thrombolytic trials have also shown a survival benefit in treated patients, placebo-controlled trials are no longer considered ethical to perform. Moreover, the complications of congestive heart failure and shock, pericarditis, and ventricular arrhythmias are reduced with thrombolytic therapy. Table 1 summarizes the rationale for thrombolytic therapy in AMI. The best results following reperfusion strategies are obtained when the conditions in Table 2 are met.

To make thrombolytic therapy available to the greatest

*From the Division of Cardiology, Department of Internal Medicine, University of Michigan Medical Center, Ann Arbor. Reprint requests: Dr. Bates, 3910 Taubman Center, 1500 E Medical Center Drice, Ann Arbor 48109

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number of patients in the briefest time, IV therapy, not intracoronary therapy, must be used. Only two trials have directly compared patency rates following IV infusion of the 2 clinically available agents, streptokinase and tPA (Table 3). At every interval from symptom onset to time of treatment, tPA achieves patency rates superior to those of streptokinase. \(^{17,18}\) Although the effect of the 2 agents on preservation of LV function has not been directly compared, the results of several studies suggest that both preserve LV ejection fraction by 5–10 percentage points vs placebo-treated patients. The 2 agents have not been directly compared in large randomized mortality studies, although this currently is being done in the GISSI-2 and ISIS-3 trials. Pooling of the small randomized trials, however, suggests that higher patency rates following tPA may result in lower in-hospital mortality than seen following streptokinase therapy\(^{17–20}\) (Table 4). That infarct artery patency alone might convey a survival benefit independent of myocardial salvage is a newer concept that has received increasing attention since the ISIS-2 trial showed a 5-week survival benefit for patients treated up to 24 h after symptom onset,\(^{21}\) a period long after that within which significant myocardial salvage is thought to occur.

### INFARCT ARTERY PATENCY AND LONG-TERM SURVIVAL

Although long-term mortality is surely related to LV ejection fraction after AMI\(^{24}\) (Fig 2), and salvaging ischemic myocardium is an important goal in treating patients, restoring infarct artery patency alone also seems to convey a long-term survival benefit independent of myocardial salvage (Table 5). In both the Western Washington intracoronary streptokinase trial\(^{20}\) and the TIMI-I trial,\(^{22}\) this benefit was evident even though there was no difference in ventricular function between treated patients and control subjects. The results are remarkably similar to those found in the Netherlands trial,\(^{13}\) where patients were treated almost 2 h sooner and preservation of LV function was shown.

Several possible explanations exist for this finding. First, arterial patency seems to favorably improve infarct healing. Reperfused myocardium did not undergo infarct expansion and aneurysm formation as did nonperfused myocardium in a rat model where infarct sizes were equivalent.\(^{25}\) The result is a decrease in systolic volume, a potent predictor of survival in both rat studies\(^{26}\) and human studies.\(^{27}\) DeFeyter et al\(^{27}\) have shown in man that chronic LV ejection fraction following AMI in conventionally treated patients is higher after spontaneous reperfusion than it is when the infarct artery remains occluded. Second, significant ventricular arrhythmias may be less frequent when arterial patency is present.\(^{28}\) Early studies suggest that sustained ventricular tachycardia is more difficult to induce in the postinfarction period, when the infarct artery is patent instead of occluded.

### Table 1—Basis for Thrombolytic Therapy

| Intra coronary thrombosis usually initiates myocardial infarction | Thrombolysis restores infarct artery patency | Arterial patency preserves left ventricular function | Left ventricular function is related to survival and quality of life |

### Table 2—Requirements for Successful Reperfusion Strategies

- Early treatment
- High and rapid reperfusion rates
- Low reocclusion rates
- Salvage of ischemic myocardium
- Avoidance of complications
- Mortality reduction

### Table 3—Patency Rates by Time to Treatment\(^*\)

<table>
<thead>
<tr>
<th>Agent</th>
<th>&lt;3 h (n = 98)</th>
<th>3–6 h (n = 313)</th>
</tr>
</thead>
<tbody>
<tr>
<td>rtPA</td>
<td>34/42 (81%)</td>
<td>109/162 (67%)</td>
</tr>
<tr>
<td>SK</td>
<td>31/56 (55%)</td>
<td>64/151 (42%)</td>
</tr>
</tbody>
</table>

\(^*\)TIMI + European Cooperative Trial.
Table 5—Early Patency and One-year Mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>IRA Patent</th>
<th>IRA Occluded</th>
</tr>
</thead>
<tbody>
<tr>
<td>WWICST</td>
<td>5.4</td>
<td>14.5</td>
</tr>
<tr>
<td>TIMI-I</td>
<td>8.1</td>
<td>14.8</td>
</tr>
<tr>
<td>Netherlands</td>
<td>4.5</td>
<td>25</td>
</tr>
</tbody>
</table>

IRA = infarct-related artery

which may reduce risk of postinfarction sudden death.\textsuperscript{19,20} Third, postinfarction ischemia may be reduced when perfusion occurs antegrade through a patent infarct artery as opposed to when perfusion to the infarct zone is dependent on collateral circulation. Satler et al\textsuperscript{19} demonstrated increased LV functional reserve following isoproterenol infusion in successfully reperfused patients. Moreover, many patients undergo definitive revascularization with coronary angioplasty or bypass graft surgery following thrombolytic therapy. Guerci et al\textsuperscript{21} showed that reducing the residual stenosis with angioplasty following reperfusion (Fig 3) restored a normal exercise-induced increase in ejection fraction, whereas patients not undergoing angioplasty had a flat or ischemic ejection fraction response. Finally, a patent artery can serve as a source for collateral blood flow later, should another artery become critically compromised, or it can be an additional site for a bypass graft, allowing more complete revascularization of a diseased circulation. Aggressive thrombolytic therapy and coronary revascularization has produced over a 90% infarct artery patency rate at hospital discharge in two studies and resulted in a 1-year cardiac mortality rate following MI of only 2%\textsuperscript{22,24} compared with the predicted rate of approximately 7–10% (Table 6).

THROMBOLYTIC THERAPY

Indications

Thrombolytic therapy has become the standard of care for AMI because of the overwhelming evidence supporting reduction in morbidity and mortality in treated patients. It is now medically and legally appropriate to consider for thrombolytic therapy every patient with AMI and to document in the medical record the reasons for treating or not treating. Patients with ischemic chest pain from 20 min to at least 6 h in duration not quickly relieved by nitroglycerin who have an injury current on their ECG are candidates for therapy, regardless of age, unless they are older than 75 years or are at increased risk for bleeding (Table 7). An accurate history and ECG interpretation are critically important in excluding patients without AMI from the bleeding risks of thrombolytic therapy. In particular, patients with aortis dissection, pericarditis, and early repolarization changes must be diagnosed correctly. Therapy should be started within 15 min of initiating patient contact; therefore, the responsibility for determining therapy will usually be that of the primary care or emergency room physician, not the cardiology consultant.

One group of patients clearly needs more definitive treatment than thrombolytic therapy alone. Patients with cardiogenic shock should be immediately referred for emergency coronary angioplasty, since it is the only form of therapy that has been suggested to reduce the 90% mortality rate that has repeatedly been demonstrated in spite of hemodynamic monitoring, inotropic support, and intra-aortic balloon counterpulsation.\textsuperscript{25} Thrombolytic therapy can be initiated if a significant delay in transfer is anticipated, but should not be considered optimal therapy.

There has been some controversy regarding treating patients with inferior infarction with thrombolytic therapy. Delayed time to treatment, low patency rates with IV streptokinase, and inadequate sample sizes have limited some of the studies.\textsuperscript{26} Patency rates are doubled in inferior infarction when tPA is substituted for streptokinase, offering the potential for an improved clinical outcome. All 8 trials that have evaluated LV function in treated patients vs controls have demonstrated higher LV ejection fractions in treated patients.\textsuperscript{26} In the ISIS-2 trial, a mortality reduction was demonstrated with streptokinase or streptokinase plus aspirin therapy.\textsuperscript{26} In the absence of other definitive mortality studies, improvement in LV function is the major justification for treating these patients. Since patients with inferior infarction and associated precordial ST segment depression in ECG leads V\textsubscript{1}-V\textsubscript{4} have a prognosis similar to that of patients

Table 6—Post-discharge One-year Cardiac Events in TAM-1 Patients (n = 387)

<table>
<thead>
<tr>
<th>Event</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>2</td>
</tr>
<tr>
<td>Recurrent MI</td>
<td>2</td>
</tr>
<tr>
<td>CABG</td>
<td>4.2</td>
</tr>
<tr>
<td>PTCA</td>
<td>4.7</td>
</tr>
</tbody>
</table>

Table 7—Indications for Thrombolytic Therapy

| Ischemic chest pain 20 min to 6 h unrelieved by NTC  
| ST segment elevation ≥0.1 mV in 2 contiguous leads  
| Low risk for bleeding |
with average-sized anterior infarction, it seems reasonable to treat them aggressively within 6 h of symptoms’ onset. Patients without reciprocal changes or hemodynamic instability, however, usually do well and probably should not be treated if they present later than 3 h, because it is unlikely that ventricular function will be improved.

Contraindications

Therapeutic benefit has not yet been demonstrated in patients with ST segment depression instead of ST segment elevation, so those patients should not routinely be subjected to the risks of treatment. Also, therapy is only recommended for patients with less than 6 h of symptoms based on data from the GISSI trial, although recent data suggest that further investigation is necessary to evaluate possible survival benefit from restoring infarct artery patency after the likelihood of myocardial salvage has passed. The major contraindication for thrombolytic therapy consists of situations in which bleeding risk is increased (Table 8). Because bleeding can cause severe complications, it is reasonable to try to obtain informed consent from the patient or family for the medical record.

Table 8—Contraindications for Thrombolytic Therapy

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute internal hemorrhage</td>
</tr>
<tr>
<td>Bleeding diathesis</td>
</tr>
<tr>
<td>History of CVA</td>
</tr>
<tr>
<td>Major surgery or trauma within 10 days</td>
</tr>
<tr>
<td>Recent puncture in noncompressible site</td>
</tr>
<tr>
<td>Traumatic CPR</td>
</tr>
<tr>
<td>Uncontrolled hypertension (&gt;180/110 mm Hg)</td>
</tr>
<tr>
<td>Intracranial or intraspinal disease</td>
</tr>
<tr>
<td>Clouded sensorium</td>
</tr>
</tbody>
</table>

Thrombolytic Agents

Thrombolytic agents dissolve thrombi by activating plasminogen, thereby generating plasmin, a plasma protein that lyses fibrin and degrades fibrinogen, prothrombin, and activated clotting factors V and VIII. Streptokinase and urokinase convert both circulating and fibrin-bound plasminogen to plasmin, producing low levels of circulating fibrinogen and high titers of fibrinogen degradation products that have prolonged anticoagulant properties. Therefore, a low fibrinogen level can be used as a clinical marker of a systemic lytic state. In contrast, tPA preferentially activates fibrin-bound plasminogen without creating a systemic lytic state as severe or prolonged as the other agents. At the most commonly used clinical doses (Table 9), however, bleeding complications between agents are equivalent.

Because streptokinase is a foreign protein obtained from bacterial cultures of streptococci, allergic reactions can occur, including fever, drug rash, and, rarely, anaphylactic shock. Streptococcal antibody titers rise within a few days, making repeated dosing unwise because of lower efficacy and more frequent side effects. Hypotension is another side effect associated with streptokinase therapy. Aggressive fluid therapy or a decrease in rate or dose of the streptokinase infusion usually are required to normalize blood pressure.

Table 9—Intravenous Thrombolytic Agents

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dosage and Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptokinase (Streptase, Kabikinase)</td>
<td>1.5 x 10^8 units over 30-60 min</td>
</tr>
<tr>
<td>Tissue plasminogen activator (Activase)</td>
<td>6-10-mg bolus with 60 mg over first hr, 20 mg over second hr, and 20 mg over third hour</td>
</tr>
<tr>
<td>Urokinase (Abbokinase)</td>
<td>1-1.5 x 10^8 units as bolus, 1-1.5 x 10^8 units over 60 min</td>
</tr>
</tbody>
</table>
Urokinase causes allergy in approximately 2% of patients; tPA infusions are not associated with allergic reactions or hypotension. High-dose urokinase and tPA yield 50% higher patency rates than streptokinase, but the price of the therapy is more than 10 times as great.

Complications

Thrombolytic therapy is changing the natural history of AMI. Congestive heart failure, pericarditis, and particularly cardiogenic shock are becoming less frequent, whereas postinfarction ischemia and bleeding have become more frequent. There was initial concern that reperfusion increased acute ventricular arrhythmias, but careful monitoring has revealed no change in overall incidence compared with untreated patients.\(^5\) No treatment is usually required for accelerated idioventricular rhythms. Reperfusion in inferior infarction can elicit reflex bradycardia and hypotension (Bezold-Jarisch reflex).\(^6\) Metaraminol (Aramine) 2.5-5 mg injected IV quickly reverses the hemodynamic abnormalities. Bundle-branch block and third-degree AV block can resolve quickly following successful reperfusion, so the need for temporary pacing in the coronary care unit will probably be decreased. Late appearance of these conduction problems after the patient has been stabilized, however, usually means reocclusion of the infarct artery. Reocclusion will occur in 10-20% of patients regardless of reperfusion strategy and is twice as likely when the right coronary artery is the infarct artery as when the left anterior descending artery is involved.\(^7\) Reocclusion risk is highest in the first 24 h after thrombolytic therapy and is unpredictable by any clinical criteria.\(^8\)

In the absence of arterial puncture, bleeding occurs in fewer than 10% of patients and is seldom serious or life-threatening. The one catastrophic bleeding complication is hemorrhagic stroke, which will occur once in every 200-250 patients treated regardless of thrombolytic agent. Risk is increased in patients with a history of previous stroke or with uncontrolled hypertension at time of presentation, so they should not be treated with the thrombolytic drugs. Another high-risk group is elderly women with low body weight and a history of hypertension and/or diabetes.\(^9\) The risk of stroke, however, needs to be placed in the context of the incidence of stroke in untreated patients with AMI. Embolic stroke from mural thrombi occurred in as many as 2% of patients when prolonged bed rest without anticoagulation was prescribed as treatment several years ago. Conversely, the incidence of hemorrhagic stroke is increased in any patient anticoagulated with heparin or given antiplatelet therapy with aspirin.\(^10\) The ISIS-2 trial\(^11\) and the ASSET trial\(^12\) recently reported that whereas the incidence of hemorrhagic stroke was increased in treated patients, embolic stroke was more frequent in control patients. There was no statistically different incidence of total stroke in the study groups. Therefore, stroke has always complicated AMI, but the etiology has changed as treatment has changed. Careful selection of patients for thrombolytic therapy is mandatory to minimize risk of stroke, but this complication is not common and should not dissuade physicians from aggressively employing thrombolytic therapy because of the important reduction in morbidity and mortality it can produce in AMI.

### Table 10—Adjunctive Drug Therapy

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose/Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA</td>
<td>1 tab po qd</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>5 mg IVP + 3, 50-100 mg BID</td>
</tr>
<tr>
<td>Heparin infusion</td>
<td>Delay until at least 1 h after tPA infusion initiated or until fibrinogen &gt; 100 mg/dl after streptokinase or urokinase</td>
</tr>
<tr>
<td>NTG infusion</td>
<td>Diltiazem 30-60 mg qid</td>
</tr>
</tbody>
</table>

### Adjunctive Treatment

Adjunctive drug therapy has empirically been administered to patients treated with thrombolytic agents (Table 10). Aspirin and heparin have been used to inhibit platelet function. The ISIS-2 trial\(^13\) suggests that 1 aspirin tablet should be ingested immediately. In this study, 160 mg of aspirin was given in chewable form at the time of entry and then daily for 30 days. Reduction in mortality of 20% was additive to the similar reduction in mortality seen with IV streptokinase therapy. Alka-Seltzer, the aspirin product used in the VA Cooperative trial in unstable angina,\(^14\) is a practical vehicle because it dissolves in water and can be easily swallowed. Heparin has routinely been infused, although there is no clear proof that it adds therapeutic benefit to the antiplatelet effect of aspirin alone. The patients in the GISSI-2 and ISIS-3 trials are being randomized to treatment with heparin or to placebo after thrombolytic therapy to answer this question. It has been shown that the heparin infusion can be delayed until after the first hour of the tPA infusion.\(^15\) Likewise, heparin ought to be delayed after treatment with streptokinase or urokinase until the fibrinogen level is over 100 mg/dl to decrease bleeding complications. Heparin infusions to increase the PTT to 1.5-2 times baseline are given for 3-7 days, with shorter infusions given to patients who have the residual stenosis reduced with early angioplasty. \(\beta\)-Blocker therapy, most commonly with low-dose IV metoprolol, may decrease infarct size by reducing oxygen demand or may prolong the time window for achieving myocardial salvage with thrombolytic therapy.\(^16\) A calcium channel blocker, usually diltiazem, is often given to inhibit increased coronary tone or spasm in the early phase following thrombolysis.

Minimizing bleeding risk needs special emphasis in the nursing orders (Table 11). Venous and arterial punctures should be avoided during the thrombolytic state. Antacids or \(H_2\) antagonists should be given to decrease GI bleeding risk. Puncture sites should be observed for bleeding and all excretions monitored for occult blood. Neurologic assessments are required to detect signs of intracranial bleeding. Because significant retroperitoneal bleeding can go unde-
Table 12—Benefits of Emergency Cardiac Catheterization

<table>
<thead>
<tr>
<th>Benefit</th>
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<tbody>
<tr>
<td>Define infarct artery perfusion status</td>
</tr>
<tr>
<td>Immediate detection of high-risk coronary</td>
</tr>
<tr>
<td>anatomy</td>
</tr>
<tr>
<td>Facilitate infarct artery patency (5-10%)</td>
</tr>
<tr>
<td>Emergency PTCA for occluded infarct arteries</td>
</tr>
<tr>
<td>Decrease in-hospital ischemic events</td>
</tr>
<tr>
<td>Permit early discharge</td>
</tr>
</tbody>
</table>

tected, the hematocrit reading must be followed routinely.

Performing 24-h ambulatory monitoring to screen for complex ventricular ectopy and a submaximal treadmill test to screen for ischemia, before discharging the patient on a β-blocker to reduce postdischarge mortality, have been standard care for several years. The very low risk for postdischarge mortality following aggressive revascularization of the infarct artery. However, suggests that the clinical benefit of ambulatory monitoring and prophylactic β-blockade should be reevaluated in the reperfusion era. The exercise test remains useful in planning revascularization attempts.

**CARDIAC CATHETERIZATION**

Cardiac catheterization is increasingly being performed routinely on patients following MI. It is usually performed before hospital discharge, with some centers doing the catheterization acutely, before the patient is admitted to the coronary care unit. Although bleeding complications are increased with emergency cardiac catheterization in the thrombolytic state, valuable prognostic information regarding hemodynamics, LV function, valvular function, and coronary anatomy can be obtained. Acute coronary arteriography (Table 12) allows early determination of infarct artery perfusion status, and the contrast injections can facilitate reperfusion by dislodging thrombus. Significant left main disease or severe 3-vessel coronary artery disease can immediately be diagnosed so that emergency or early coronary bypass graft surgery can be planned. Persistent occlusion of the infarct artery can be treated with emergency angioplasty. Patients with insignificant residual stenoses or low-risk anatomy can be mobilized early and discharged from the hospital after a short stay. Immediate or early revascularization with angioplasty or surgery probably decreases postinfarction ischemic events and may also permit early discharge from the hospital.

**CORONARY ANGIOPLASTY AND SURGERY**

Three recent trials have demonstrated that angioplasty immediately following thrombolytic therapy with tPA is associated with lower success rates, higher complication rates, and higher mortality rates than a delayed angioplasty strategy, without additional improvement in LV ejection fraction. Thus, for general clinical purposes, it does not appear that every patient with AMI must be emergently transferred to a tertiary care center for immediate angioplasty. Emergency transport systems must be in place, however, to transfer subgroups of patients for acute angioplasty (Table 13). In particular, patients in cardiogenic shock should undergo immediate attempts at angioplasty. Likewise, patients with large infarcts, significant congestive heart failure, or hemodynamic compromise should be considered for emergency transfer.

There may be a role for performing "rescue" angioplasty in patients who fail thrombolytic therapy. This strategy would be more practical if there were a noninvasive clinical means of determining successful reperfusion. Unfortunately, relief of chest pain, normalization of elevated ST segments, and bursts of ventricular arrhythmias inconsistently occur following successful reperfusion so there appears to be no accurate way to determine thrombolytic failure short of coronary arteriography. Rescue angioplasty, therefore, is limited to the minority of patients who undergo acute catheterization.

Postinfarction angina or an ischemic exercise test response before hospital discharge are other important indications for performing coronary angioplasty. Direct angioplasty is also an important treatment option in patients with contraindications for thrombolytic therapy.

Bypass graft surgery will probably play an increasing role in patients with AMI. Emergency surgery for patients with multivessel disease and cardiogenic shock or life-threatening anatomy (ie, right coronary artery occlusion and severe left main artery disease) is being attempted at some centers. Surgery within a week of AMI can now be safely accomplished with current techniques and was performed in 20% of the patients in the TAMI-I trial.

**EXPENSE**

Tissue plasminogen activator, urokinase, cardiac catheterization, coronary angioplasty, and bypass graft surgery are expensive treatment modalities that are not fully covered under current reimbursement plans. The cost of using these treatments in patients with AMI, however, is similar to the cost of treating patients with chronic renal failure, cancer, or other significant medical diseases. Moreover, many of the patients treated are relatively young and can return to full, productive lifestyles.

Use of tPA has made it unnecessary to transfer most patients with AMI by helicopter to regional centers, allowing the use of much cheaper ground transportation to electively transfer selected patients for early cardiac catheterization. Cardiac catheterization and angioplasty in the first few days of hospitalization permit early hospital discharge in some patients, which can further reduce cost. The low incidence of cardiac events in the year following hospital discharge after aggressive reperfusion for AMI may mean fewer clinic and emergency room visits, lower hospitalization rates, less diagnostic testing, and reduced medication requirements. Furthermore, the impressive decrease in mortality and heart failure rates with these interventions should reduce life insurance, social security, disability, and welfare payments to families who can return wage earners to gainful employment. The full costs to the health care system remain...
to be determined but will certainly be expensive. Reimbursement plans will need to be rapidly adjusted to ensure that all appropriate patients will have access to these beneficial interventions.

**CONCLUSION**

Early thrombolytic therapy and aggressive coronary revascularization have dramatically changed the prognosis in patients with AMI. Coronary care units and the electrical defibrillator reduced in-hospital mortality rates from 30% to 15% 20 years ago, but no further improvement was realized until thrombolytic therapy was advanced. Now the in-hospital mortality rates following thrombolytic therapy are 4-5%. Moreover, mortality in the year following hospital discharge has been reduced from approximately 10% to 2% by maintaining infarct artery patency and relieving postinfarction ischemia in many patients by angioplasty or bypass graft surgery. Very successful public education programs have been waged against cigarette smoking, hypertension, and hypercholesterolemia. It is now time to educate the public about the symptoms of AMI and to encourage early evaluation, so that the benefits of electrical defibrillation, thrombolytic therapy, and coronary revascularization can be made available to as many patients as possible.

**REFERENCES**

36 Tissue Plasminogen Activator in Cardiopulmonary Disease

284S


