A Prospective, Placebo-Controlled, Randomized Trial of Intravenous Streptokinase and Angioplasty Versus Lone Angioplasty Therapy of Acute Myocardial Infarction

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**Background.** The value of routine administration of intravenous thrombolytic agents during percutaneous transluminal coronary angioplasty (PTCA) therapy of acute myocardial infarction (MI) has not been determined. Therefore, we prospectively randomized 122 patients with evolving MI to PTCA therapy with or without adjunctive intravenous streptokinase therapy.

**Methods and Results.** Patients with ECG ST segment elevation who presented within 4 hours of symptom onset, had no contraindication to thrombolytic therapy, and were not in cardiogenic shock were enrolled. They were treated immediately with intravenous heparin (10,000 units) and oral aspirin (325 mg) and randomized to treatment with placebo or streptokinase (1.5 M units) administered intravenously over 30 minutes. Patients then were taken immediately to the catheterization laboratory, and those with suitable coronary anatomy underwent immediate PTCA. Subsequent clinical course, serial radionuclide ventriculography, and 6-month repeat angiography were analyzed. A total of 106 patients were treated with PTCA. Use of PTCA was similar for placebo (92%) and streptokinase (83%) groups. Angioplasty was successful in 95% of patients, with no difference in placebo (93%) and streptokinase (98%) groups. Serial radionuclide ventriculography demonstrated no difference in 24-hour (52±12% versus 50±12%) or 6-week (51±12% versus 51±13%) ejection fraction values for placebo and streptokinase groups, respectively. Contrast ventriculography demonstrated improvement in immediate (54±12% versus 6-month (60±15%, p<0.05) values for the overall group. No differences in 6-month values were present (58±15% versus 62±15%, p=NS) for placebo and streptokinase groups, respectively. Coronary angiography was performed in 75% of the 90 patients eligible for restudy. Arterial patency was 87% at 6 months, and coronary restenosis was present in 38% of patients. No differences in chronic patency or restenosis were detected for the two treatment groups. Although adjunctive intravenous streptokinase therapy did not improve outcome, it did complicate the hospital course. Hospitalization was longer (9.3±5.0 versus 7.7±4.4 days, p=0.046) and more costly ($25,191±15,368 versus $19,643±7,250, p<0.02). Transfusion rate was higher (39% versus 8%, p=0.001) and need for emergency coronary bypass surgery was greater (10.3% versus 1.6%, p=0.03) for the streptokinase-treated patients.

**Conclusions.** Adjunctive intravenous streptokinase therapy does not enhance early preservation of ventricular function, improve arterial patency rates, or lower restenosis rates after PTCA therapy of acute MI. Hospital course is longer, more expensive, and more complicated. For these reasons, PTCA therapy of acute MI should not be routinely performed with adjunctive intravenous streptokinase therapy.


**Key Words** • percutaneous transluminal coronary angioplasty • streptokinase • clinical trials • myocardial infarction • reperfusion • thrombolytics

The modern era of invasive reperfusion therapy of acute myocardial infarction was ushered in by the studies of Khaja et al1 and Anderson et al.2 These randomized trials demonstrated that intracoronary streptokinase could induce coronary recanalization in a majority of cases. Shortly thereafter, Kennedy et al3 demonstrated that intracoronary streptokinase therapy improved survival. Interest in invasive reperfusion therapy was increased when we4 demonstrated that angioplasty therapy was more effective than use of...
intracoronary streptokinase in preserving ventricular function and decreasing postinfarction angina.

Although intracoronary streptokinase and coronary angioplasty appeared to be effective, the need for emergency catheterization limited applicability of either strategy. Thus, widespread use of reperfusion therapy did not occur until intravenous streptokinase was shown to decrease mortality. Although intravenous therapy was widely applicable, there remained concern about the potentially deleterious impact of the residual stenosis remaining after thrombolytic therapy. For this reason, the role of sequential intravenous thrombolytic therapy followed immediately by angioplasty was explored. Topol et al found that no benefit was derived from routine angioplasty in patients who had already achieved arterial patency through thrombolytic therapy. More recently, investigators of the Thrombolysis in Myocardial Infarction Trial (TIMI) reported that routine angiography and angioplasty did not improve outcome compared with thrombolytic therapy alone. Based on these recent studies, many investigators have concluded that the role for invasive reperfusion therapy is limited.

Although there now can be no question that intravenous thrombolytic therapy is most widely applicable, a role for invasive reperfusion therapy may still exist. Centers with facilities and expertise can achieve excellent clinical results with angioplasty therapy. This form of therapy may be particularly effective when thrombolytic therapy is contraindicated. In addition, thrombolytic therapy has had disappointing results for patients in cardiogenic shock. Angioplasty therapy may offer a survival advantage for these high-risk patients. Before angioplasty therapy can have a defined clinical role, further prospective evaluation of this therapy is necessary. Despite a 10-year history of angioplasty therapy of myocardial infarction, a paucity of prospective clinical trials of this therapy exists. Although combined therapy with intravenous thrombolytic agents and angioplasty has had extensive prospective evaluation, lone angioplasty therapy has not been evaluated thoroughly. To this end, we report results of a prospective, randomized clinical trial of lone angioplasty therapy compared with combined intravenous thrombolytic therapy and angioplasty. The purpose of this study was to determine whether adjunctive intravenous thrombolytic therapy optimizes preservation of ventricular function after angioplasty therapy. In addition, we evaluated the impact of thrombolytic therapy on hospital course, chronic arterial patency, and restenosis.

**Methods**

**Patient Selection**

Between July 1988 and March 1990, patients with evolving acute myocardial infarction were prospectively recruited for this study. Patients were treated at William Beaumont Hospital, Royal Oak, Mich., or Moses Cone Memorial Hospital, Greensboro, N.C. Institutional review board permission for conduct of these studies was obtained at both institutions. Signed, informed consent was obtained from the patients or immediate relatives. Entry criteria similar to those of contemporaneous US thrombolytic trials were used; patients were 18–76 years old, had chest discomfort lasting >30 minutes that was unresponsive to sublingual nitroglycerin, and presented within 4 hours of symptom onset. A transmural injury pattern (ST segment elevation in two contiguous leads of $\geq 0.2$ mV or mirror findings of posterior injury) was required. Patients with ECG left bundle branch block pattern or previous Q wave myocardial infarction in the presumed jeopardized territory were excluded. Patients also were excluded if they had contraindications to thrombolytic therapy as outlined by the TIMI-IIIB trial. Finally, patients with an admission systolic blood pressure $\leq 80$ mm Hg that was unresponsive to volume challenge also were excluded.

**Treatment Protocol**

After informed consent was obtained, 10,000 units heparin i.v. and 325 mg aspirin p.o. were administered. Oxygen therapy at 2–4 I/min by nasal cannula was administered. Intravenous morphine sulfate (2–4 mg) or meperidine HCl (50–75 mg) was administered as needed for analgesia. Intravenous xylocaine HCl (150 mg over 15 minutes and a 2–4 mg/min infusion) was initiated. Patients were taken immediately to the catheterization laboratory. All patients were pretreated with 50 mg diphenhydramine HCl i.v. Study medication (1.5 million units streptokinase or placebo infusion) was administered over 30 minutes. Low-molecular-weight dextran (40 ml/hr) was administered for 24 hours. Selective coronary angiography of the noninfarct-related artery first and the presumed infarction-related artery second was performed. Ventriculography was performed in the right anterior oblique projection using 0.5–0.7 ml/kg of contrast. Ventriculography was not performed if left ventricular end-diastolic pressure was $>25$ mm Hg. Videotape replay of the coronary angiograms was used for initial angiographic analysis. Patients were excluded from angioplasty therapy if a left main stenosis $>70\%$ was present, if the infarction was due to occlusion of a small distal branch of a major epicardial vessel, if the infarct-related artery could not be clearly identified, or if the infarct artery was patent with severe diffuse disease. Otherwise, angioplasty was performed regardless of the patency status of the vessel.

At the initiation of the angioplasty procedure, an additional dose of 5,000 units heparin was administered. Intravenous verapamil (5 mg) was administered if systolic blood pressure was $>90$ mm Hg. Intracoronary nitroglycerin (250 $\mu$g) was selectively infused just before PTCA.

After catheterization, all patients were treated with continuous intravenous heparin titrated to maintain the activated clotting times at $\geq 180$ seconds for 24 hours. Vascular sheaths were removed 24 hours after the catheterization. Heparin therapy was transiently interrupted before sheath removal. Once hemostasis was achieved, heparin was readministered for an additional 3–5 days. All patients were treated with intravenous nitroglycerin for 24 hours. Dosage was titrated to decrease systolic blood pressure by $\geq 10$ mm Hg. Aspirin (325 mg daily) and diltiazem (30–60 mg q.i.d.) were administered orally. Laboratory evaluation including complete blood count, fibrinogen, and creatine phosphokinase isoenzymes were obtained every 6 hours for 24 hours. Patients had radionuclide ventriculograms 24–36 hours after admission. Rest and exercise-gated blood pool images were obtained at 6 weeks after...
therapy. Before discharge, symptom-limited exercise thallium scintigraphy was performed.

Contrast ventriculograms were analyzed by one investigator who was blinded to the randomization assignment. The 30° right anterior oblique end-diastolic and end-systolic endocardial silhouettes were outlined using a light-pen system. The ventricular volumes and ejection fractions were calculated using the area-length method. Regional wall motion of the infarct and noninfarct zones was determined by the centerline chord method as described by Sheehan et al.18 Similarly coronary arteriograms were analyzed by the same blinded investigator. A single view that most clearly identified the affected coronary segment was chosen. Quantitative coronary arteriography was obtained using the Artrek computerized edge detection method developed by LeFree et al.19 Angioplasty was considered to be successful if quantitative percent diameter stenosis of <50% was achieved after angioplasty. Similarly, coronary restenosis was defined as described by Serruys et al20 as a final diameter stenosis >50% at the time of the repeat catheterization. Identical coronary angiographic views were used in the initial catheterization and at the repeat catheterization for determination of restenosis. Repeat cardiac catheterization was performed on all eligible patients who provided separate informed consent. At the time of repeat catheterization, contrast ventriculography was again performed in the 30° right anterior oblique projection. Coronary arteriography was performed in multiple projections. Before arteriography, 250 µg nitroglycerin i.c. was infused.

Statistical Analysis

Sample size was estimated to demonstrate a 5% difference in ejection fraction between the two groups. Based on this assumption, 49 evaluable ventriculograms would provide a power of 0.9. All continuous variables were analyzed by Student's t test, and dichotomous variables were analyzed by χ² tests. A value of p ≤ 0.05 was considered statistically significant.

Results

During the enrollment period, 122 patients with evolving acute myocardial infarction met inclusion criteria and consented to participate in this clinical trial. Patients were randomized to placebo or adjunctive streptokinase therapy and taken immediately to the catheterization laboratory. Catheterization was not delayed for initiation of intravenous study medication. One patient with unstable hemodynamics rapidly developed cardiogenic shock and electromechanical dissociation in the emergency ward before catheterization could occur. The remaining 121 patients underwent catheterization (Figure 1). At the time of catheterization, one of the investigators determined angiographic eligibility for angioplasty. All physicians were blinded to the identity of study medications throughout the catheterization.

Baseline Descriptors

Treatment groups were analyzed to ensure comparable severity of illness (Table 1). Age, sex, medication use, and ECG myocardial infarction location were similar for the treatment groups. Of the relevant clinical history, only incidence of previous myocardial infarction differed, with placebo patients having a higher incidence of previous myocardial infarction. Although the placebo group presented significantly later (83±41 versus 69±39 minutes, p = 0.049), time to initiation of intravenous therapy was similar (160±52 versus 175±57 minutes, p = 0.13). To further ensure comparability of treatment groups, catheterization descriptors were analyzed (Table 2). No differences were detected in

![Figure 1. Flow chart of angiographic exclusions for percutaneous transluminal coronary angioplasty (PTCA) where present in 15 patients; they included left main stenosis >50%, left main equivalent disease, or lesion with <50% luminal narrowing. ER, emergency room.](image-url)
TABLE 2. Baseline Catheterization Descriptors for Patients Treated With Angioplasty and Streptokinase or Placebo

<table>
<thead>
<tr>
<th></th>
<th>Streptokinase</th>
<th>Placebo</th>
<th>p</th>
</tr>
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<tbody>
<tr>
<td>Systolic pressure (mm Hg)</td>
<td>136±21</td>
<td>133±25</td>
<td>0.55</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>76±16</td>
<td>75±20</td>
<td>0.98</td>
</tr>
<tr>
<td>LVEDP (mm Hg)</td>
<td>22.5±6.5</td>
<td>22.5±8.0</td>
<td>0.99</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>51±14</td>
<td>52±12</td>
<td>0.66</td>
</tr>
<tr>
<td>TIMI I/I flow (% patients)</td>
<td>81</td>
<td>76</td>
<td>0.330</td>
</tr>
<tr>
<td>TIMI II/III flow (% patients)</td>
<td>19</td>
<td>24</td>
<td>0.330</td>
</tr>
<tr>
<td>Diseased vessels</td>
<td>1.8±0.8</td>
<td>1.7±0.7</td>
<td>0.42</td>
</tr>
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bpm, Beats per minute; LVEDP, left ventricular end-diastolic pressure; TIMI, Thrombolysis in Myocardial Infarction Trial.

systolic blood pressure, heart rate, left ventricular end-diastolic pressure, or contrast ejection fraction. At the time of baseline angiography, 78% of the patients had TIMI 0 or I flow.21 No differences were detected in initial arterial patency between treatment groups. The low rate of arterial patency percentage in the streptokinase-treated group reflects the speed with which catheterization was performed; 23 of 58 streptokinase-treated patients (40%) had arterial access and baseline angiography before streptokinase therapy could be initiated. The mean time from onset of streptokinase therapy to baseline angiography was 31±21 minutes for the remaining 35 patients.

Results of Intervention

Overall, 86% of the treatment group underwent coronary angioplasty (Table 3). A trend toward increased use of angioplasty was present in the placebo group (81% versus 92%, p=0.08). Angioplasty was not performed in the streptokinase patients because of severe, diffuse multivessel disease in four patients, lack of critical lesions in three patients, and inability to clearly delineate the culprit artery in three patients. Similarly, angioplasty was not performed in the placebo-treated patients because of severe diffuse disease in four patients and lack of identifiable infarct artery in one patient. Technically, angioplasty was associated

TABLE 3. Comparison of Patients With and Without Serial Paired Contrast Ventriculograms

<table>
<thead>
<tr>
<th>Ventriculograms</th>
<th>Paired</th>
<th>Not paired</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>55</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>54±10</td>
<td>55±11</td>
<td>0.55</td>
</tr>
<tr>
<td>Male (%)</td>
<td>84</td>
<td>91</td>
<td>0.4</td>
</tr>
<tr>
<td>First MI (%)</td>
<td>89</td>
<td>83</td>
<td>0.6</td>
</tr>
<tr>
<td>Successful PTCA (%)</td>
<td>96</td>
<td>97</td>
<td>0.7</td>
</tr>
<tr>
<td>Time to reperfusion (minutes)</td>
<td>182±59</td>
<td>207±55</td>
<td>0.04</td>
</tr>
<tr>
<td>Treated with streptokinase (%)</td>
<td>44</td>
<td>40</td>
<td>0.7</td>
</tr>
<tr>
<td>MI location (n) (%)</td>
<td>25/55 (45)</td>
<td>15/35 (43)</td>
<td>0.75</td>
</tr>
<tr>
<td>Anterior</td>
<td>3/55</td>
<td>4/35 (11)</td>
<td></td>
</tr>
<tr>
<td>Posterior</td>
<td>26/55</td>
<td>15/35 (43)</td>
<td></td>
</tr>
<tr>
<td>Inferior</td>
<td>1/55</td>
<td>1/35 (3)</td>
<td></td>
</tr>
<tr>
<td>Baseline ejection fraction (%)</td>
<td>53±12</td>
<td>51±13</td>
<td>0.52</td>
</tr>
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MI, myocardial infarction; PTCA, percutaneous transluminal coronary angioplasty.

FIGURE 2. Bar graph of early radionuclide study performed 24 hours after therapy showed no difference between placebo (52±12%) and streptokinase (SK) groups (52±12%) (p=NS). Convalescent study also showed no difference between placebo (51±12%) and SK groups (51±13%) (p=NS). Analysis of paired studies also failed to demonstrate serial improvement in ventricular function. PTCA, percutaneous transluminal coronary angioplasty.

with a high degree of technical success. Angioplasty was successful in 99 of 104 patients (95%) and was equally successful regardless of whether lone angioplasty (93%) or adjunctive streptokinase (98%) was used.

Serial Arteriographic and Ventriculographic Changes

The primary end point of this trial was to determine whether adjunctive streptokinase therapy had an impact on ventricular function compared with lone angioplasty treatment. To this end, serial radionuclide and contrast ventriculograms were obtained. Radionuclide ejection fraction values at 24 hours after admission were 52±12% for the lone angioplasty group and 50±12% for the streptokinase group (p=NS). Similarly, convalescent values at 1 month were no different (51±12% versus 51±12%, p=NS) for lone PTCA and streptokinase groups, respectively. No early improvement in ventricular function was detected for either subgroup (Figure 2). Late changes in ventricular function were analyzed using paired contrast ventriculography. Serial contrast ventriculograms of sufficient technical quality for analysis were obtained in 55% of the 90 patients discharged alive who did not undergo bypass. To ensure that selection bias did not occur for patients having adequate quality ventriculograms, detailed analysis of patients with or without adequate serial studies was performed (Table 3). Successful reperfusion was achieved in 96% of patients with paired studies and 97% of patients without paired studies. Of importance is that baseline ventricular function was similar for both groups. Reperfusion time was slightly later in patients without paired studies. Figure 3 depicts the major improvement in global ventricular function that occurred for the entire cohort (54±12% versus 60±15%, p<0.01). Although ventricular function was improved for the entire group, no difference in convalescent ejection fraction between streptokinase and lone PTCA subgroups occurred (59±15% versus 62±14%, p=NS). Regional wall motion of the infarct zone was analyzed by centerline chord method. A trend toward less hypokinesis for the streptokinase group in initial study (−2.80±1.8 versus −2.15±2 SD/chord, p=NS) and in the convalescent study (−0.71±2.27 versus 0.14±2.40...
SD/chord, p=NS) was present. Analysis of serial paired studies showed a significant improvement in regional function over the 6-month follow-up for both placebo (p<0.001) and streptokinase (p<0.001) groups.

Coronary arteriography at 6 months demonstrated an overall patency rate of 87%. No difference in patency was observed for the PTCA-alone group (89%) compared with the streptokinase group (86%, p=0.5). Restenosis defined as ≥50% stenosis as assessed by quantitative angiography was 37% for the PTCA-alone group and 31% for the streptokinase group (p=0.46).

Clinical Course

In addition to assessing the impact of adjunctive thrombolytic therapy on ventricular function and arterial patency, the clinical course of the two groups was analyzed (Table 4). The in-hospital clinical course appeared to be worsened by the use of adjunctive thrombolytic therapy. A significantly higher rate of bleeding complications and vascular surgical complications occurred in patients treated with streptokinase. One patient in the streptokinase group had an intracerebral hemorrhage. Systemic bleeding (genitourinary, 1.7%; gastrointestinal, 5.2%; oral, 1.7%; and central nervous system, 1.7%) was present in the streptokinase patients but did not occur in the lone-PTCA-treated patients. Vascular surgical repair was required in three streptokinase-treated patients (5.2%) and none of the lone-PTCA group. Major hematomas occurred in nine streptokinase patients (15.5%) and two in the lone-PTCA group (3%). Hospital stay was more prolonged for the streptokinase-treated patients (9±5 versus 7.7±4 days, p=0.03). Review of hospital charges demonstrated that total charges for the lone-PTCA group were lower than that for the streptokinase group. One cost outlier was present in the streptokinase group. This patient had a complicated 6-month hospitalization related to intracranial hemorrhage and accrued a hospital bill of $471,000. When he was removed from analysis, the mean charge for the streptokinase group was $25,191 ± 15,368 compared with $19,643 ± 7,250 (p<0.02) for the lone-PTCA group. Most disturbing was the fact that a higher need for coronary bypass within 4 days of admission was present for the streptokinase-treated patients (10.5% versus 1.6%, p<0.03). Overall, eight streptokinase-treated patients required urgent bypass. In three patients, reocclusion refractory to prolonged balloon inflation occurred. In three patients, severe diffuse three-vessel disease with ongoing ischemic pain was present, requiring immediate bypass surgery. The final two patients had bypass on day 4 because of recurrent angina in the face of severe three-vessel disease. In comparison, only one patient in the lone-PTCA group required bypass. This was required on an emergency basis for occlusive dissection. The use of adjunctive thrombolytic agents was associated with a lower nadir hemoglobin level (9.2 versus 10.3 g, p<0.001) and a greater need for blood transfusions (39% versus 8%, p<0.001). Although hospital course was lengthier, more complicated, and more costly for streptokinase-treated patients, rate of reinfarction and mortality was similar for both groups.

Discussion

Although there is an abundance of data concerning the efficacy of combined thrombolytic and angioplasty therapy of acute myocardial infarction,7,22–24 there is a paucity of prospectively collected data on lone-angioplasty therapy.25 At the present time, angioplasty combined with antecedent thrombolytic therapy is considered inferior to thrombolytic therapy alone.26 This

![Figure 3](http://circ.ahajournals.org/)

**FIGURE 3.** Bar graph of contrast ejection fraction values were compared for streptokinase (SK) and lone-angioplasty patients. No differences were apparent between the two groups. PTCA, percutaneous transluminal coronary angioplasty.

![Figure 4](http://circ.ahajournals.org/)

**FIGURE 4.** Bar graph of changes in regional wall motion (RWM) determined by centerline chord method were assessed by streptokinase (SK) and lone-angioplasty patients. Infarct zone function improved in both groups of patients. PTCA, percutaneous transluminal coronary angioplasty.
conclusion is based on the lack of proven superiority of combined therapy in decreasing mortality or preserving myocardial function while perhaps increasing mortality in the aggressively treated patients.22,24 On the other hand, the addition of thrombolytic therapy may worsen the results of angioplasty therapy. Waller et al27 demonstrated that intramural hemorrhage is present in blood vessels treated with angioplasty and thrombolytic therapy. Pavilides et al28 observed that major cardiac events occur more frequently in patients with coronary dissection after PTCA who are treated with intracoronary thrombolytic therapy. In addition to deleterious local effects, thrombolytic agents have been shown to activate platelets through a thrombin-mediated pathway,29,30 which may lead to an increased rate of abrupt closure. Conversely, a systemic fibrinolytic state theoretically could decrease abrupt closure by providing an antiplatelet effect through generation of fibrin degradation products.31,32 In view of these complex competing influences, the only way to determine the value or harm of adjunctive thrombolytic therapy was through a prospective, randomized trial.

In the present study, patient enrollment criteria were the same as contemporaneous US thrombolytic trials. The overall mortality rate of 5.7% in the present study is equal to that of these trials. The sample size of this study obviously is too small to make conclusive statements in this regard. Ultimately, a large mortality trial of angioplasty versus intravenous thrombolytic therapy will be required. Before conduct of such a mortality trial, we felt obliged to determine the optimal aggressive strategy. The end points of ventricular function were chosen in the present study not as surrogates for mortality but rather to magnify the major potential advantage of intravenous thrombolytic therapy. This presumed advantage is the potential earlier administration of a thrombolytic agent compared with invasive therapy. Earlier therapy should lead to more myocardial salvage and more effectively preserved myocardial function. This belief prompted the design of the TIMI and Thrombolysis in Acute Myocardial Infarction (TAMI) trials to study sequential intravenous thrombolytic therapy followed by PTCA without ever testing lone-PTCA therapy. In the present study, we attempted to administer both thrombolytic and PTCA therapy as rapidly as possible. We found that 40% of patients had PTCA initiated before intravenous thrombolytic therapy was initiated. Although intravenous therapy should save time to initiation of therapy, major time delays still occur.33,34 In centers such as ours where catheterization facilities are readily available, time delay in initiation of PTCA therapy may be less than that for initiation of intravenous thrombolytic therapy. Because no time advantage was achieved, it is not surprising that no difference in global ventricular function was detected by sequential radionuclide ventriculography. A major improvement in global and regional ventricular function was detected at the 6-month repeat catheterization as has previously been demonstrated.13 No advantage existed for additional use of thrombolytic therapy. The findings of this study relating to ventricular function must be tempered by the sample size. A trend did exist toward more effective preservation of regional function at 6-month follow-up for the streptokinase-treated patients (+0.3±1.5 versus −0.5±1.5 SD/chord, p=NS). A sample size of 61 patients in each group would have been necessary to detect a 1-SD/chord difference. In addition, therapy was initiated relatively late in this study. The benefits of prehospital thrombolytic therapy or thrombolytic therapy administered within 60 months of symptom onset have not been addressed. For this reason, the ability of very early adjunctive streptokinase therapy to preserve convalescent regional function has not been definitively precluded by this clinical trial.

Another major objective of this study was to determine if systemic thrombolytic therapy altered the procedural outcome or clinical course. No differences in mortality, reinfarction, or postinfarction angina were detected. Although only a small number of patients needed emergency bypass surgery for failed PTCA therapy, a greater need for bypass was present in the streptokinase-treated patients. The rate of emergency bypass surgery in streptokinase-treated patients is similar to that reported by Topol et al7 for recombinant tissue-type plasminogen activator (rt-PA)—treated patients. It appears that both clot-selective and systemic thrombolytic agents increase the need for emergency bypass surgery after infarct angioplasty. Further deleterious effects of streptokinase therapy included a higher transfusion requirement and more prolonged hospital stay. Bleeding complications were similar in number to those reported by Topol et al7, TIMI Research Group,22 and Stack et al35 for patients treated with streptokinase or rt-PA. We have demonstrated that bleeding complications are lower for lone-PTCA therapy than for adjunctive thrombolytic therapy. Furthermore, the catastrophic risk of intracerebral hemorrhage is not an issue with lone-PTCA therapy. These findings suggest that lone-PTCA therapy may be ideally suited for patients who might be at risk of hemorrhage with thrombolytic therapy.

Finally, the impact of thrombolytic therapy on coronary reocclusion and restenosis was analyzed. The 6-month arterial patency rate of 87% was not affected by additional streptokinase therapy. Although reocclusion rates appear lower for systemic thrombolytic agents36,37 than for fibrin-specific agents, no benefit is achieved by adding a systemic thrombolytic agent to PTCA therapy. In addition to reocclusion, restenosis rates for patients treated with lone-PTCA therapy were comparable to those treated with adjunctive intravenous streptokinase therapy. The fibrin and platelet deposition that occurs on infarct-related arteries may enhance propensity for restenosis after angioplasty therapy. In fact, the known higher rates of restenosis in patients with unstable angina38,39 may in part be related to these and other hemostatic constituents that are deposited on sites of local arterial injury. Unfortunately, the present study demonstrates that application of intravenous systemic thrombolytic therapy does not lessen the risk of restenosis of infarct-related arteries.

Conclusions

In hospitals with readily available catheterization facilities, no value is derived from the adjunctive use of thrombolytic agents for patients undergoing PTCA therapy of acute myocardial infarction. Ventricular function is not incrementally augmented by the use of streptokinase. No decrease in reocclusion or reinfarc-
tion rates occurs. Streptokinase, if anything, worsens clinical outcome because it is associated with more local and systemic bleeding complications, prolonged hospital course, and greater hospitalization costs. Late arterial patency and restenosis are not altered by adjunctive streptokinase therapy. Thus, patients chosen for emergency PTCA therapy should have this therapy without intravenous streptokinase therapy. The major relevance of this finding is that emergency PTCA therapy can be used optimally without thrombolytic therapy. This fact will expand the eligibility for reperfusion therapy to patients who are ineligible for thrombolytic therapy due to risk of hemorrhage. Cragg et al previously demonstrated that 15% of myocardial infarction patients are excluded from thrombolytic therapy due to potential bleeding risks. This subgroup would be ideally suited for lone-PTCA therapy. The major clinical question of whether lone-PTCA therapy is comparable or superior to lone thrombolytic therapy remains to be answered by prospective, randomized trials. For now, we have determined that an optimal aggressive interventional strategy requires deletion of routine adjunctive intravenous thrombolytic therapy.

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Circulation. 1992;86:1710-1717
doi: 10.1161/01.CIR.86.6.1710

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1992 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

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