THE ROLE OF PERCUTANEOUS TRANSLUMINAL CORONARY ANGIOPLASTY IN THE PATIENT WITH ACUTE MYOCARDIAL INFARCTION

Richard A. Lange, M.D.

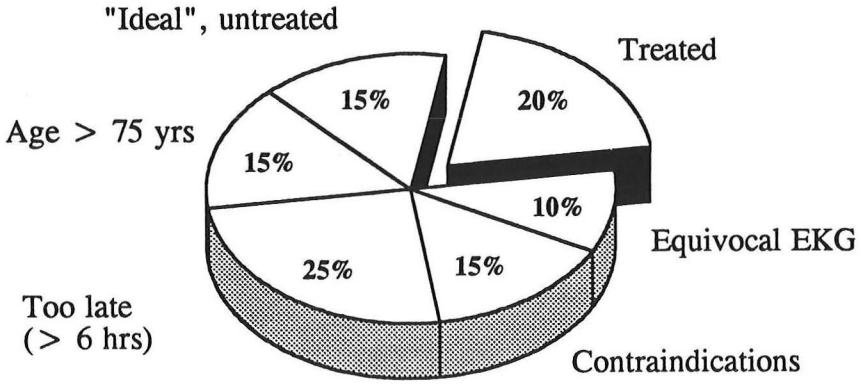
Internal Medicine Grand Rounds
University of Texas Southwestern Medical Center at Dallas
Dallas, Texas

February 24, 1994

Almost fifteen years ago, DeWood and colleagues showed that cardiac catheterization was feasible in patients with acute myocardial infarction [1]. Their study and subsequent angiographic and postmortem studies demonstrated that occlusive coronary thrombus was the cause of most Q-wave myocardial infarctions. Accordingly, the focus of attention in the treatment of acute myocardial infarction has been the use of thrombolytic agents. Many large trials have shown that thrombolytic agents restore patency in occluded coronary arteries and improve left ventricular function and survival in patients with evolving Q-wave myocardial infarction [2-5].

However, there are several limitations to the use of thrombolytic agents. First, many patients with acute myocardial infarction do not receive thrombolytic therapy because they have a contraindication to its administration or are not thought to benefit from its use (Figure 1). Of the 625,000 Americans who have an acute myocardial infarction annually in the United States, only 122,000 receive thrombolytic therapy [6].

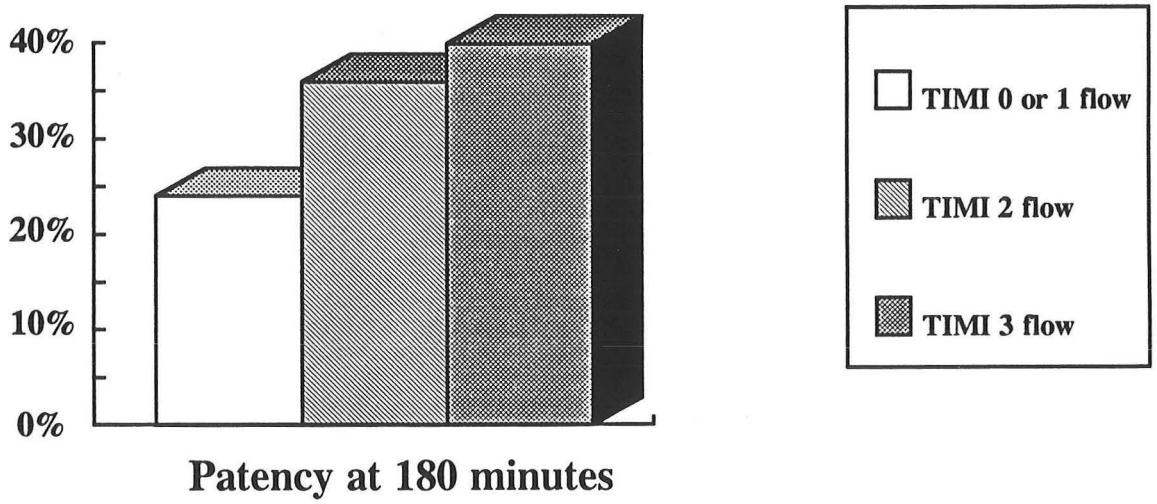
Figure 1. The Percentage of Patients Eligible and Ineligible For Thrombolysis According to Current Recommendations and Practices [6]



Second, bleeding complications and cerebrovascular accidents may occur in those who receive thrombolysis. In the recent GUSTO (Global Utilization of Streptokinase vs tPA for Occluded Coronaries) megatrial which examined the use of streptokinase, tissue plasminogen activator, or both in over 40,000 patients with acute myocardial infarction, 5-6% of those who received thrombolysis had moderate bleeding, approximately 0.5% experienced a severe or life threatening bleeding episode and 1.5% of the patients had a cerebrovascular accident [7].

Third, thrombolytic agents are unsuccessful in achieving early reperfusion in many patients. In the GUSTO trial [8], a subset of the patients had serial angiograms demonstrating that many who receive a thrombolytic achieve no or only partial antegrade perfusion (Figure 2).

Figure 2. Infarct Artery Patency After Administration of a Thrombolytic in the GUSTO Angiographic Substudy



Definitions: TIMI 0 = no antegrade perfusion; TIMI 1 = penetration without perfusion; TIMI 2 = partial perfusion; TIMI 3 = complete perfusion.

Fourth, severe residual coronary stenoses are often present in those in whom thrombolysis is successful and may lead to recurrent ischemia, recurrent myocardial infarction. In the GUSTO trial [7], 40% of patients had recurrent ischemia during their hospitalization and 3% experienced reinfarction. In the subset of patients who had serial coronary arteriograms, almost 7% of those with antegrade coronary flow 90 minutes after thrombolysis had no reoccluded within 1 week [8].

Thus, while thrombolytic therapy has proven useful in improving left ventricular function and survival in patients with acute myocardial infarction, there are limitations to its applicability and efficacy. Consequently, several prospective, randomized trials have assessed the role of percutaneous transluminal coronary angioplasty in the patient with evolving myocardial infarction.

The Role of PTCA in the Patient With Acute Myocardial Infarction

1. Reduce residual stenosis following successful thrombolysis
2. Restore flow following unsuccessful thrombolysis ("salvage" PTCA)
3. Use instead of thrombolysis ("primary" PTCA)

In the immediate period following the onset of myocardial infarction, PTCA has been used (a) to relieve a high-grade residual stenosis of the infarct artery after successful thrombolysis, (b) to restore antegrade coronary flow in the patient in whom thrombolysis is unsuccessful (so-called "salvage" or "rescue" PTCA), or (c) instead of thrombolytic therapy to restore antegrade flow in the infarct artery (so-called "primary" PTCA). The practicing physician is often uncertain if the patient with acute myocardial infarction should be treated at, or subsequently transferred to, a facility where PTCA is available. Therefore, this review will focus on the role of PTCA as adjunctive or primary therapy in the patient with acute myocardial infarction.

I. Routine PTCA Following Successful Thrombolysis

Occlusive coronary thrombus and subsequent myocardial infarction occur when platelets and fibrin aggregate at sites of endothelial injury or atherosclerotic plaque rupture [9]. For several days after successful fibrinolysis, platelet aggregation and thrombus formation may recur at the site of arterial injury and lead to reocclusion, especially if a severe residual stenosis is present [10]. Hence, many physicians perform catheterization on all patients who have received thrombolysis, with the intention of performing PTCA if a high-grade residual stenosis is present. This is done in hopes of preventing reocclusion, reinfarction, and death. In this setting, PTCA may be performed immediately (within hours), early (within 2 days), or late (up to 2 weeks) after thrombolytic therapy.

A. PTCA of a Stenotic Infarct Artery Immediately After Thrombolysis

Three randomized, prospective trials have examined the efficacy and safety of immediate PTCA after administration of tissue plasminogen activator (tPA) (Table 1).

Table 1. Trials of Immediate PTCA Following Successful Thrombolysis

Study (ref)	No. pts	Timing of immediate PTCA	Timing of deferred PTCA
TIMI IIA [11]	389	< 2 hrs	18 to 48 hrs
TAMI-I [12]	367	< 90 min	7 to 10 days
ECSG-VI [13]	197	< 3 hrs	"conservative" management

Abbreviations: ECSG = European Cooperative Study Group; TAMI = Thrombolysis in Acute Myocardial Infarction; TIMI = Thrombolysis in Myocardial Infarction

In the Thrombolysis in Myocardial Infarction IIA (TIMI IIA) study, 389 patients who received tPA were randomly assigned to immediate (within 2 hours) or delayed (18 to 48 hours) PTCA of the infarct artery [11]. Left ventricular function (assessed by radionuclide ventriculography), the study's primary endpoint, was similar for the 2 groups at hospital discharge (Table 2). However, those who underwent immediate PTCA had an *increased* incidence of cardiac catheterization or PTCA related complications (new coronary occlusion, arrhythmia, pulmonary edema, hypotension, cardiac arrest, or anaphylaxis), blood transfusions, coronary artery bypass surgery, and overall major adverse events (death, recurrent myocardial infarction, emergent coronary artery bypass surgery, or transfusion).

Table 2. Results of the TIMI-IIA Study [11]

	Immediate PTCA (< 2 hrs)	Delayed PTCA (18-48 hrs)
No. pts	195	194
No. PTCA	141 (72)	107 (55)
PTCA success	119 (84)	100 (94)
LVEF (pre discharge)	0.50	0.49
21 day mortality	14 (7)	11 (6)
Cath/PTCA complication	24 (12)	7 (4)*
CABG	32 (16)	15 (8)*
Blood transfusion	39 (20)	14 (7)**

* $p < 0.01$; ** $p < 0.001$

Numbers in parenthesis represent percentages

The Thrombolysis in Acute Myocardial Infarction (TAMI-1) study examined 197 patients who underwent routine PTCA of a stenotic infarct artery immediately (90 minutes) or 7 to 10 days after thrombolytic therapy [12]. Left ventricular ejection fraction at 1 week -- the primary endpoint of the study -- was similar for the 2 groups, as was the incidence of reocclusion (Table 3). Left ventricular ejection fraction at 6 months was also similar for both groups [14]. Notably, 18% of the patients required a transfusion of $\geq$ 2 units of blood, with most bleeding occurring at the site of vascular access.

Table 3. Results of the TAMI-I Study [12]

	Immediate PTCA (< 90 min)	Delayed PTCA (7-10 days)
No. pts	99	98
No. PTCA	99 (100)	51 (52)
PTCA success	84 (85)	47 (92)
Reocclusion	11 (11)	13 (13)
LVEF (pre discharge)	0.53	0.56
In-hospital mortality	4 (4)	1 (1)
Emergent CABG	7 (7)	2 (2)*
Blood transfusion	Overall 18%	

Numbers in parenthesis represent percentages

A similar outcome was noted in the European Cooperative Study Group VI trial [13], in which 367 patients who received thrombolytic therapy were randomized to immediate PTCA or conservative management, with cardiac catheterization and PTCA only for those with spontaneous or provocable ischemia (Table 4). Immediate PTCA successfully reduced the residual stenosis in the infarct artery; however, this was offset by a high rate of transient (16%) and sustained (7%) reocclusion during the procedure and recurrent ischemia during the first 24 hours. Immediate PTCA

did not influence myocardial infarct size -- as measured enzymatically or by left ventricular ejection fraction -- nor the subsequent incidence of reinfarction. Those who underwent immediate angioplasty had a higher incidence of recurrent ischemia, bleeding complications, and transfusions. The study was prematurely terminated because those who underwent immediate PTCA had a higher early (2 week) mortality than those managed conservatively. At 1 year, the mortality remained higher in those who had immediate PTCA (9.3 vs. 5.4%)[15].

Table 4. Results of the ECSG-VI Study [13]

	Immediate PTCA (< 2 hrs)	No PTCA
No. pts	183	184
No. PTCA	168 (92)	NR
PTCA success	149 (89)	NR
LVEF (pre discharge)	0.51	0.51
Reinfarction	12 (7)	8 (4)
Recurrent ischemia (24h)	31 (17)	6 (3)*
Bleeding complication	75 (41)	43 (23)*
In-hospital mortality	13 (7)	6 (3)*
Emergent CABG	3 (2)	0 (0)
Blood transfusion	18 (10)	7 (4)*

Numbers in parenthesis represent percentages
* reported to be significantly different, but p values not provided

Taken together, these trials show no benefit of routine PTCA of the stenotic infarct artery in the early hours after thrombolytic therapy. Such a strategy does not appear to salvage myocardium or prevent reinfarction or death. On the contrary, patients subjected to this approach appear to have an *increased* incidence of adverse events, including bleeding, recurrent ischemia, emergent coronary artery bypass surgery, and death.

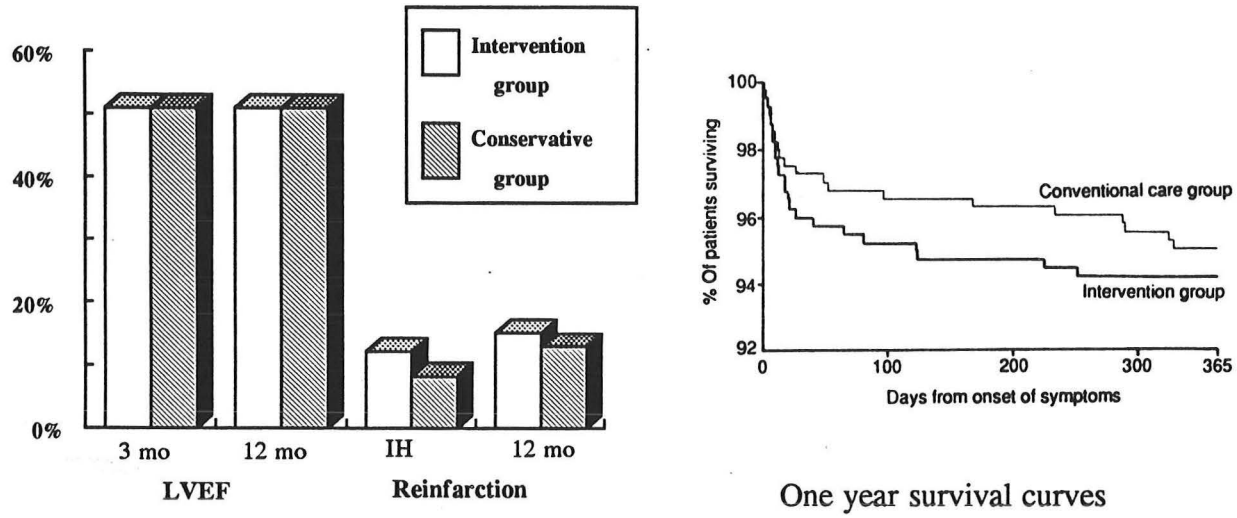
Recent studies have provided insight into why routine PTCA immediately following thrombolysis may be deleterious. Excessive bleeding and transfusion requirements in these patients are usually the result of vascular complications at the site of catheterization. In addition, when PTCA is performed after thrombolytic therapy, there is more extensive hemorrhage into the vessel wall than when either treatment is used alone [16, 17]. This may further compromise the lumen of the infarct artery and promote rethrombosis and reocclusion.

B. PTCA of a Stenotic Infarct Artery Early (Hours to Days) After Thrombolytic Therapy

It has been suggested that elective PTCA of the stenotic infarct artery hours to days after thrombolysis may allow sufficient time for development of a more stable hemostatic milieu at the site of the coronary lesion. In this setting, PTCA would be safer and more effective in reducing the incidence of reocclusion and improving survival. Two large randomized, prospective trials have tested this hypothesis, with both concluding (a) that there are fewer complications if PTCA is delayed for several days following thrombolytic therapy and (b) that routine PTCA in the absence of spontaneous or provocable ischemia does not improve left ventricular function or survival.

In the British SWIFT (Should We Intervene Following Thrombolysis) Study [18], 800 patients with acute myocardial infarction who received intravenous APSAC were randomized to PTCA within 2 to 7 days or to "conservative" management, with catheterization and PTCA only for spontaneous or provocable ischemia. Only 3% of patients in the "conservative" group had coronary angioplasty and 2% underwent coronary bypass grafting during the initial admission. There was no difference between the 2 treatment strategies with regard to left ventricular function (at 3 or 12 months), incidence of reinfarction (in-hospital and 1 year), or survival (in-hospital and 1 year) (Figure 3).

Figure 3. Major Endpoints of the SWIFT Trial [18]



One year survival curves

Abbreviations: IH = In-hospital

The TIMI IIB trial [19] randomized 3262 patients who had received tissue plasminogen activator to routine catheterization and PTCA within 18 to 48 hours of thrombolysis or conservative management. At the end of the 6 week follow-up period, the 2 groups had a similar mortality, incidence of nonfatal reinfarction, and left ventricular ejection fraction (Table 5). At 1 year, survival, anginal class, and frequency of bypass surgery were similar in the 2 groups [20]. Two- and three-year results were recently published [21] and demonstrate that the mortality and reinfarction rates in the two strategies remain comparable over long-term follow-up (Figure 4). Thus, in unselected patients receiving thrombolytic therapy, PTCA of the stenotic infarct artery within several days does not appear to be beneficial.

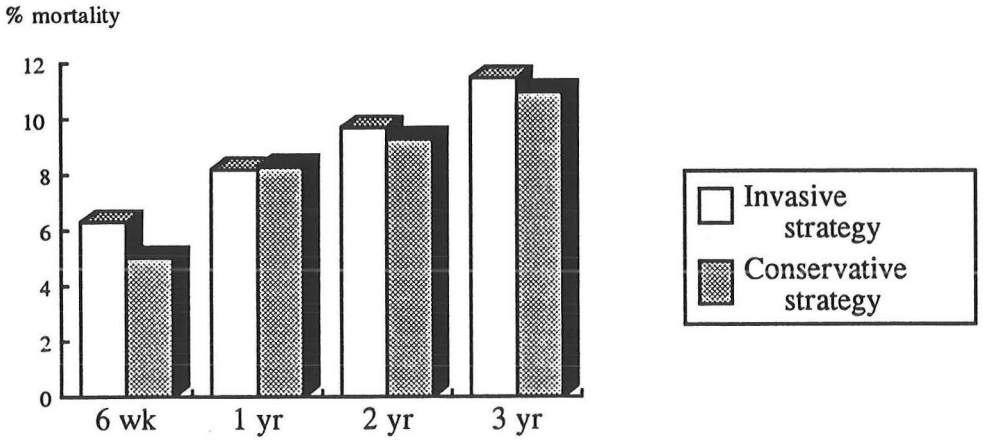
Table 5. TIMI-IIB Results: 6 Week Endpoints and Clinical Events [19]

Invasive Strategy	Endpoint	Conservative Strategy
0.50	LVEF	0.50
6.4%	Reinfarction	5.8%
17%	Positive exercise test	19%
5.2%	Mortality	4.7%
13.0	Any adverse outcome**	10.6%*
16%	Transfusion	13%*

* $p < 0.05$

** Any adverse outcome combines death, nonfatal reinfarction, intracranial hemorrhage, and coronary artery bypass grafting after PTCA

Figure 4. TIMI IIB Trial: Long-term Mortality Data [21]



C. "Late" PTCA of the Stenotic Infarct Artery (Days to Weeks) After Thrombolytic Therapy

Continued clot lysis and remodeling of the infarct artery stenosis occurs over the days to weeks after successful thrombolysis, making the underlying residual coronary stenosis more "stable" and less prone to rethrombosis and reocclusion. Thus, delaying PTCA for days to weeks after thrombolysis might improve survival even though earlier routine PTCA does not. Two studies have tested this hypothesis. In one, patients with post-infarction angina or provocable ischemia were excluded from randomization, whereas in the other they were included in the study.

Trials of "Late" PTCA of the Stenotic Infarct Artery

Study	No. pts	Timing of PTCA	Post-MI angina or ischemia
Barbash et al [22]	201	> 72 hrs	Yes
TOPS [23]	87	4-14 days	No

Barbash et al [22] randomized 201 patients treated with tissue plasminogen activator to (a) catheterization and PTCA of suitable lesions - including occluded vessels - more than 72 hours after admission or (b) conservative management, with revascularization only for recurrent ischemia. The groups had similar left ventricular function at 2 month follow-up (0.51 for both), rates of reinfarction (16 and 12%, respectively), and mortality at 10 months (8% and 4%, respectively). Ellis et al [23] also assessed late PTCA following thrombolytic therapy in the Treatment of Post-Thrombolytic Stenoses (TOPS) Study. Following intravenous thrombolysis, Ellis and colleagues randomly assigned 87 asymptomatic patients to PTCA at 4 to 14 days or conservative management. Those with postinfarction angina or ischemia with provocative testing were excluded. Although those having PTCA had less angina at 1 year, there was no difference in survival in the 2 groups.

Procedure-related infarction occurred in 9.5% of patients, which is similar to that observed when mechanical revascularization is attempted earlier in the post infarction course [19,24].

In short, ***routine*** PTCA of the stenotic infarct artery during the hours, days, or weeks following thrombolytic therapy exerts no benefit in comparison to conservative management. The former is associated with an increased incidence of local vascular complications, blood transfusions, and emergent coronary artery surgery, with no demonstrable improvement in left ventricular function, incidence of reinfarction, or survival. Therefore, an invasive strategy should be reserved for survivors of infarction who manifest ischemia at rest or with provocation.

II. PTCA Following Failed Thrombolysis

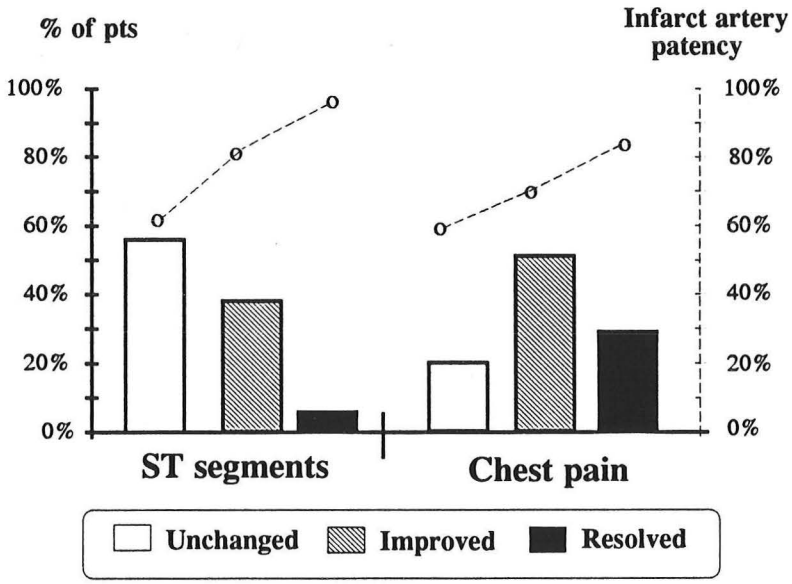
Intravenous thrombolytic therapy is successful in restoring antegrade coronary flow in 75 to 90% of patients with acute myocardial infarction [25,26]. In the 10 to 25% in whom it is unsuccessful, antegrade coronary flow can usually be restored with PTCA. This may be performed immediately after unsuccessful thrombolysis (so called "salvage" or "rescue" PTCA) or over the subsequent hours to days.

A. "Salvage" PTCA of a Persistently Occluded Infarct Artery Immediately After Failed Thrombolysis

Several studies have demonstrated the marked beneficial effect of infarct artery patency (obtained via endogenous, pharmacologic, or mechanical recanalization) on survival in patients with acute myocardial infarction [27-30]. Survivors of myocardial infarction with a patent infarct artery have an improved long-term outcome in comparison to those whose infarct artery is occluded, even though left ventricular systolic function is similar [30,31]. In the 10 to 25% of patients in whom thrombolytic therapy fails to restore antegrade coronary flow, recanalization of the infarct artery via PTCA has been advocated (a) to establish early infarct artery patency, (b) to salvage ischemic (but viable) myocardium, and (c) to improve long-term survival. Unfortunately, no large randomized trial has assessed the effects of early salvage PTCA (performed immediately after identification of failed thrombolysis) on left ventricular function, subsequent cardiac events, or mortality.

A major obstacle in adopting a strategy of salvage PTCA lies in the timely and accurate identification of patients in whom thrombolytic therapy has failed to reestablish antegrade coronary flow. Unless unsuccessful thrombolysis is recognized and rectified quickly (within 3 to 6 hours of the onset of symptoms), salvage of ischemic myocardium is unlikely. Unfortunately, clinical markers of reperfusion -- relief of chest pain, resolution of ST segment elevation, and reperfusion arrhythmias -- have limited predictive value in identifying failure of thrombolysis (Figure 5) [32]. For example, 16 to 25% of patients with resolution of chest pain, normalization of ST segment changes, or reperfusion arrhythmias after thrombolytic therapy have a persistently occluded infarct artery.

Figure 5. Relation of Traditional Predictors of Reperfusion to Observed Patency of the Infarct-Related Artery [32]



Immediate catheterization of all patients following thrombolytic therapy to identify those with an occluded infarct artery is impractical, costly, and often associated with bleeding complications [11, 12]. In the future, real time 12 lead electrocardiographic monitoring of ST segments [33] or analysis of serum concentrations of myoglobin or creatine kinase isoforms that rise early after recanalization [34] may provide a noninvasive assessment of infarct artery patency and permit identification of patients most likely to derive benefit from mechanical recanalization after unsuccessful thrombolysis.

Limitations of "Salvage" PTCA

1. No reliable method to assess infarct-artery patency
2. Time delay
3. High failure/reocclusion rate
4. High mortality if unsuccessful
5. Delayed spontaneous reperfusion in many patients

Even in the patient with documented failure of thrombolysis, it is unknown if salvage PTCA should be attempted. First, since extensive myocardial necrosis occurs when coronary occlusion has been present for > 3 hours [35], salvage PTCA may not save a substantial amount of myocardium, considering the time delay associated with presentation of the patient to the hospital after symptom onset, infusion of the thrombolytic agent, recognition of failed thrombolysis, and initiation of salvage PTCA. Second, salvage PTCA is ineffective in reestablishing antegrade coronary flow in approximately 15% of patients, and reocclusion of the infarct artery occurs in 20% of the remainder [28]. Third, unsuccessful salvage PTCA is associated with a high (up to 44%) mortality [27]. Finally, coronary reperfusion occurs over the subsequent hours in many patients whose infarct artery is occluded early after receiving a thrombolytic agent. Although infarct artery patency 90 minutes after thrombolytic therapy is only 65 to 75%, it rises to 90% by 24 hours [26]. Such "late" reperfusion may improve survival without the risk of invasive procedures coupled with thrombolytic therapy.

Recent nonrandomized and retrospective studies have suggested that mechanical reperfusion of occluded coronary arteries may improve survival in patients with myocardial infarction and cardiogenic shock [36-41]. Such patients have a hospital survival of only about 20% when treated with intravenous thrombolytic therapy [42]. Conversely, mechanical restoration of antegrade coronary flow via PTCA is associated with a hospital survival of about 70% in these patients (Table 6). Multicenter, prospective, randomized studies are currently underway to verify these promising results, and the Parkland Memorial Hospital Cardiac Catheterization Laboratory is participating in one under the direction of Dr. John Willard.

Table 6. Survival in Patients With Myocardial Infarction and Cardiogenic Shock Treated With PTCA

Study (ref)	No. Pts.	Survival with successful PTCA	Survival with unsuccessful PTCA
Ellis et al [36]	61	86%	32%
Lee et al [37]	24	77%	18%
Lee et al [38]	69	69%	20%
Moosvi et al [39]	38	56%	8%
Gacioch et al [40]	68	61%	7%
Hibbard et al [41]	45	71%	29%

Thus, until published data from randomized clinical trials show that early salvage PTCA is beneficial, this approach should not be routinely applied to all patients who seem to have failed thrombolytic therapy. However, it probably should be considered in those with cardiogenic shock and a persistently occluded infarct artery.

B. PTCA of a Persistently Occluded Infarct Artery Late (Hours to Days) After Failed Thrombolysis

Infarct artery patency is an important predictor of mortality in survivors of myocardial infarction [29,30,43-45]. In comparison to those with a patent infarct artery, survivors of infarction with an occluded artery have (a) increased left ventricular dilatation [46], (b) a greater incidence of spontaneous and inducible ventricular arrhythmias [47], and (c) a poorer prognosis [43]. In survivors of infarction, infarct artery patency may favorably influence left ventricular remodeling and electrical stability even if accomplished at a time when salvage of ischemic myocardium is unlikely (i.e., hours to days after unsuccessful thrombolysis)[48].

The utility of late PTCA of a persistently occluded infarct artery was assessed in a randomized trial -- the Thrombolysis in Acute Myocardial Infarction VI (TAMI-VI) Study -- in which rescue PTCA was performed 7 to 48 (mean, 25) hours after symptom onset [49]. Angiography 6 months later revealed a high incidence of infarct artery patency in those who did not receive PTCA as well as a high incidence of reocclusion in those who did, so that infarct artery patency was similar in the 2 groups. Not surprisingly, the 2 groups also had a similar left ventricular ejection fraction, incidence of reinfarction, hospital readmission, and mortality during follow-up.

In summary, there are no published data to support the routine use of salvage or late PTCA in all patients with failed thrombolysis. A large, prospective, multicenter trial -- the Randomized Evaluation of Salvage Angioplasty with Combined Utilization of Endpoints (RESCUE) study -- has been conducted to assess more fully the role of salvage PTCA in patients with acute myocardial infarction [50], but its results are not yet available. Until its results are published, the use of salvage PTCA must be individualized.

III. PTCA as Primary Therapy For Acute Myocardial Infarction

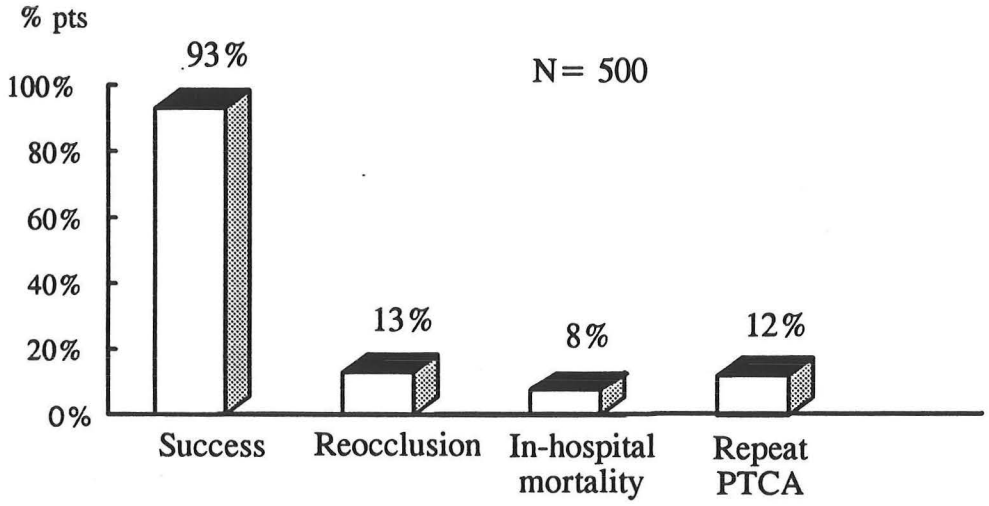
Since the original report of PTCA as an alternative to thrombolytic therapy in the patient with acute myocardial infarction [51], the merits of this approach have been debated [52,53]. Many observational series of primary PTCA report mortality rates comparable to those obtained in the thrombolytic trials (Table 7). Some advantages of catheterization and direct PTCA in the patient with acute myocardial infarction include (a) documentation of coronary occlusion in patients with equivocal electrocardiographic changes; (b) immediate documentation of reperfusion success; (c) rapid assessment of residual stenosis severity; (d) acquisition of catheterization-derived prognostic variables; and, (d) applicability to most patients with infarction, especially those who are ineligible for thrombolytic therapy.

Table 7. Observational Reports of Primary PTCA for Acute Myocardial Infarction

Study	Study period	No. pts	In-hospital mortality
Flaker et al [54]	85-88	93	14%
Marco et al [55]	publ 87	43	14%
Ellis et al [56]	83-88	271	13%
Rothbaum et al [57]	82-86	151	9%
Brodie et al [58]	84-88	383	9%
Bittle [59]	89-90	20	9%
Kahn et al [60]	81-89	614	8%
Beauchamp et al [61]	82-89	214	8%
Grines et al [62]	publ 91	58	5%
Williams et al [63]	publ 91	226	5%

Primary PTCA in patients with myocardial infarction restores antegrade flow in the occluded infarct artery in > 90% and is associated with a 1 year survival of 90 to 96% [64-67] (Figure 6). Primary PTCA for acute myocardial infarction is less likely to be successful in patients with depressed left ventricular function, three vessel coronary artery disease, or a tortuous infarct artery [68]. In addition, some data suggest that direct PTCA of the right coronary artery is more often associated with procedural complications [69,70] and reocclusion [71] when compared to PTCA of the other arteries. Predictors of improved long term survival following PTCA for acute myocardial infarction include preserved left ventricular function, a patent infarct artery at discharge, early reperfusion, and single vessel coronary artery disease [24,64,66].

Figure 6. Cumulative Experience With Primary PTCA in 500 Patients From The Mid-America Heart Institute [64]



Since both PTCA and thrombolysis effectively restore coronary flow in the majority of patients with acute myocardial infarction, the issue of which is better has sparked controversy. Three randomized trials using contemporary PTCA equipment and techniques have compared these approaches [72-74] (Table 8). In these studies, patients who presented within 6 to 12 hours of the onset of an acute myocardial infarction were randomized to routine thrombolytic therapy or catheterization and primary PTCA. In those in whom it was attempted, PTCA successfully restored antegrade coronary flow in 93 to 99% and was performed in a timely fashion (mean time from randomization to PTCA approximately 60 minutes). Of note, in those randomized to primary PTCA, the procedure was not attempted if cardiac catheterization demonstrated left main stenosis, severe three vessel disease, or "high risk" lesions. Thus, 4 to 5% of patients who were randomized to primary PTCA underwent coronary artery bypass surgery instead.

Table 8. Prospective, Randomized Trials of Primary PTCA

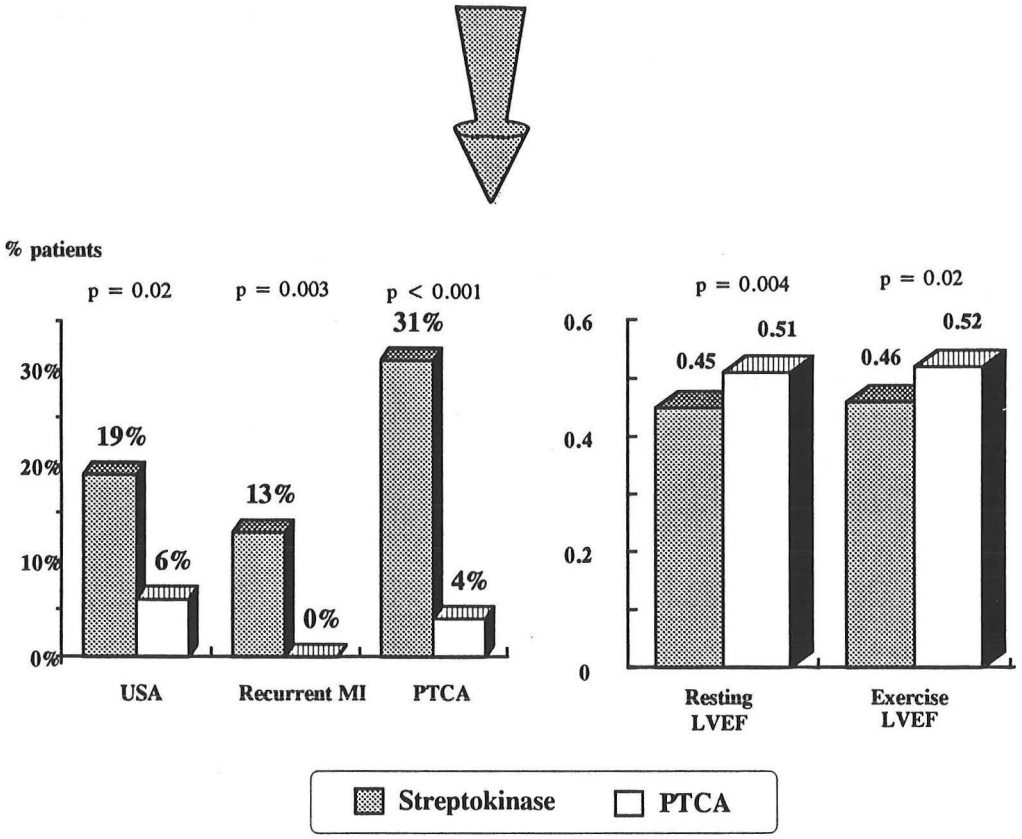
Study	No. Pts	Thrombolytic	PTCA Success	Endpoints
Netherlands Trial [72]	142	SK (1.5 mU/1h)	98%	Left ventricular function Coronary patency/stenosis Clinical events
Mayo Clinic Trial [73]	108	tPA (0.6 mg/kg/4h)	93%	Myocardial salvage Cost Clinical events
PAMI Trial [74]	395	tPA (100mg/3h)	99%	Left ventricular function Clinical events

Abbreviations: PAMI = Primary Angioplasty in Myocardial Infarction; SK = streptokinase; tPA = tissue plasminogen activator

In the Netherlands trial by Zijlstra et al [72], follow-up angiography weeks after infarction showed that the infarct artery was patent in 91% of those who had PTCA and in only 68% of those who received thrombolysis ($p = 0.001$). The residual infarct artery stenosis was also less in those who underwent PTCA (36% vs 76%, $p < 0.001$). As a result, those who underwent primary PTCA had fewer in-hospital adverse events (non-fatal reinfarction or death) and were less likely to have recurrent ischemia or require coronary revascularization over the follow-up period (Figure 7). Resting and exercise left ventricular ejection fraction (assessed by radionuclide ventriculography) was higher in those who received primary PTCA.

Figure 7. Results of Netherlands Primary PTCA Trial [72]

PTCA		Streptokinase	
91%	Infarct arteries patent	68%	p = 0.001
36%	Residual stenosis	76%	p < 0.001



In the Mayo Clinic trial, Gibbons et al [73] also found that those who underwent primary PTCA were less likely to require coronary artery revascularization for recurrent ischemia over a 6 month follow-up period than those treated with thrombolysis. Nevertheless, the two groups had similar myocardial salvage (as assessed by technetium-99m sestamibi perfusion imaging), left ventricular

ejection fraction, incidence of recurrent myocardial infarction, and survival (Figures 8 and 9). Furthermore, there was no significant monetary difference between the two treatment strategies.

Figure 8. Myocardial Salvage as a Percentage of the Left Ventricle in Patients with Anterior (n=37) and Inferior (n=62) Myocardial Infarction [73]

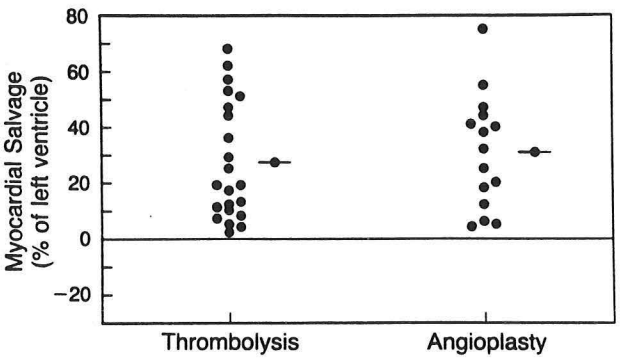


Figure 1. Myocardial Salvage as a Percentage of the Left Ventricle in Patients with Anterior Infarctions.

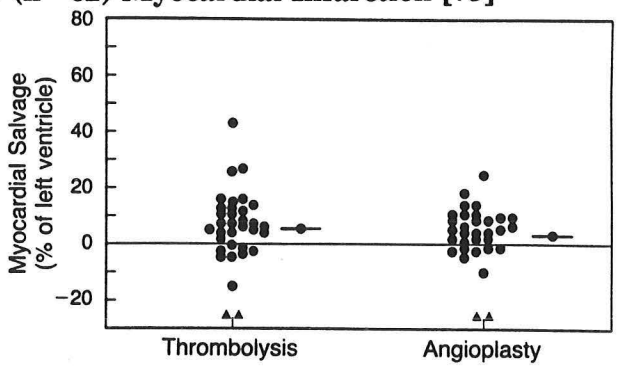


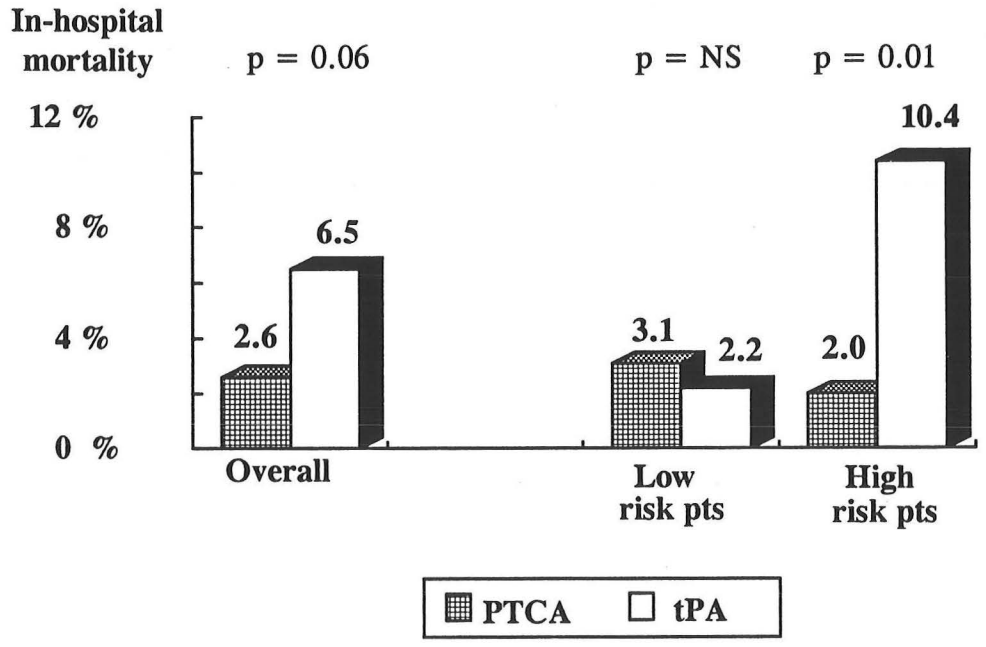
Figure 2. Myocardial Salvage as a Percentage of the Left Ventricle in Patients with Inferior Myocardial Infarctions.

Table 9. Results of the Mayo Clinic Primary PTCA Trial [73,75]

Thrombolytic therapy		Primary PTCA
15%	Myocardial salvage	13%
0.50	LV ejection fraction at 6 wks	0.53
4%	Recurrent MI	0%
0%	In-hospital mortality	2%
$1,876	Cost to salvage 1% myocardium (at 1 year, by intention to treat)	$1,431
$1,659	Cost to salvage 1% myocardium (at 1 year, by treatment received)	$1,654

These findings were confirmed by the Primary Angioplasty in Myocardial Infarction (PAMI) investigators [74], who found that PTCA offered no clear advantage in terms of left ventricular function (ejection fraction = 0.53 for both groups) or mortality with the exception of "high risk" patients (i.e., > 65 years old, anterior infarction, or tachycardia on presentation). Mortality in these patients was 2% for those who underwent PTCA and 10% for those who received thrombolysis (p = 0.01) (Figure 9). The apparent survival benefit of PTCA is, at least in part, due to the fact that the thrombolytic group had an excessive incidence of cerebrovascular hemorrhage (2%) with death; cardiac related deaths were similar in the 2 groups.

Figure 9. PAMI Trial Mortality Data [74]



In comparison to thrombolytic therapy, primary angioplasty reduces the incidence of subsequent hospital morbidity, readmission, and follow-up costs, largely by reducing recurrent ischemia following intervention. However, this benefit comes at the cost of performing PTCA on all patients presenting with infarction, rather than the 20 to 40% who required a revascularization procedure for clinical indications following thrombolytic therapy in these trials [72-74].

Before considering PTCA as the preferred therapy of acute myocardial infarction, several caveats should be kept in mind. Since only 18% of hospitals in the United States have cardiac catheterization laboratories and even fewer have the capability of performing emergent PTCA, its applicability as primary therapy for acute myocardial infarction is limited. Although the transfer of patients with myocardial infarction to facilities that can perform PTCA is possible, the obligate delay in achieving reperfusion may outweigh the potential benefits. The excellent PTCA success rates achieved by the investigators of these trials results from their extensive experience with this technique, which may not be generally available. Finally, since 5% of patients initially referred for PTCA required emergent coronary artery bypass surgery, primary PTCA should be performed in centers with experienced and immediately available cardiac surgeons.

Rationale for deciding between thrombolytic therapy or primary PTCA are presented below. Primary PTCA should be considered in patients presenting with acute myocardial infarction who have a contraindication to thrombolytic therapy. However, caution must be exercised in patients with bleeding as a contraindication to thrombolytic therapy, since PTCA mandates the aggressive use of heparin in the peri-procedural period [76]. "High risk" infarction patients and those in whom thrombolytic therapy is not beneficial should also be considered for primary PTCA.

Acute Myocardial Infarction Patients Who Should Be Considered For Primary PTCA

1. Those with a contraindication to thrombolysis

2. Those "suspected" to benefit from primary PTCA
   - elderly
   - anterior MI
   - tachycardia (large MI)

3. Those in whom thrombolytic therapy is not beneficial
   - cardiogenic shock

4. When PTCA can be performed quickly and expertly
   - no delay
   - experienced PTCA operators
   - cardiothoracic surgical backup

Acute Myocardial Infarction Patients Who Should Be Considered For Thrombolysis

1. Patients in whom PTCA is of questionable benefit
   - young
   - non-anterior MI
   - "small" MI

2. Those with a "contraindication" to PTCA
   - severe peripheral vascular disease
   - renal insufficiency
   - history of contrast allergy

3. PTCA not immediately available

4. Experienced PTCA operators not available

5. Cardiothoracic surgical backup not available

IV. Conclusions

The routine use of PTCA (a) as a salvage procedure after failed thrombolysis or (b) to improve the angiographic appearance of a residual stenosis in the infarct artery following successful thrombolysis appears not to be justified in the patient without spontaneous or provocable ischemia. This strategy provides no benefit and may even be harmful if performed within hours of infarction. Whether patients with a persistently occluded infarct artery and cardiogenic shock benefit from mechanical recanalization requires further study. Alternatively, PTCA is appropriate in the patient with post infarction angina at rest or with provocation. Thus, patients who have a myocardial infarction -- regardless of whether a thrombolytic agent has been given -- do not require transfer to a hospital with PTCA facilities unless there is a clinical indication for cardiac catheterization.

PTCA as primary therapy for acute myocardial infarction is effective in achieving recanalization but may not offer clear survival advantages over thrombolysis, except in certain "high-risk" groups [77]. Because of the limited availability of catheterization and PTCA facilities, thrombolytic therapy is likely to remain the preferred treatment in many patients with acute infarction. Primary angioplasty should be considered in the 50-60% patients who are not candidates for thrombolytic therapy [6] as well as certain "high risk" patients, provided, of course, that it can be performed quickly and expertly.

REFERENCES

1. DeWood, MA, Spores J, Notske R, et al. Prevalence of total coronary occlusion during the early hours of transmural myocardial infarction. N Engl J Med 1980; 303: 897-902.

2. Simoons ML, van der Brand M, de Zwabb C, et al. Improved survival after early thrombolysis in acute myocardial infarction. Lancet 1985; 2: 578-81.

3. GISSI Study Group. Effectiveness of intravenous thrombolytic therapy in acute myocardial infarction. Lancet 1986; 1: 397-402.

4. AIMS Trial Study Group. Effect of intravenous APSAC on mortality after acute myocardial infarction: Preliminary report of a placebo-controlled clinical trial. Lancet 1988; 1: 546-9.

5. ISIS-3 Collaborative Group. ISIS-3: A randomised comparison of streptokinase vs. tissue plasminogen activator vs. anistreplase and of aspirin plus heparin vs. aspirin alone among 41,299 cases of suspected acute myocardial infarction. Lancet 1992; 339: 753-70.

6. Muller DWM, Topol EJ. Selection of patients with acute myocardial infarction for thrombolytic therapy. Ann Intern Med 1990; 113: 949-60.

7. The GUSTO Investigators. An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. N Engl J Med 1993; 329: 673-82.

8. The GUSTO Angiographic Investigators. The effects of tissue plasminogen activator, streptokinase, or both on coronary-artery patency, ventricular function, and survival after acute myocardial infarction. N Engl J Med 1993; 329:1615-22.

9. Davies MJ, Thomas T. Plaque fissuring-the cause of acute myocardial infarction, sudden death and crescendo angina. Br Heart J 1985; 53: 363-70.

10. Harrison DG, Ferguson DW, Collins SM, et al. Rethrombosis after reperfusion with streptokinase: Importance of geometry of residual lesions. Circulation 1984; 69: 991-9.

11. The TIMI Research Group. Immediate vs. delayed catheterization and angioplasty following thrombolytic therapy for acute myocardial infarction. JAMA 1988; 260: 2849-58.

12. Topol EJ, Califf RM, George BS, et al. A randomized trial of immediate versus delayed elective angioplasty after intravenous tissue plasminogen activator in acute myocardial infarction. N Engl J Med 1987; 317: 581-8.

13. Simoons ML, Arnold AE, Betriu A, et al. Thrombolysis with tissue plasminogen activator in acute myocardial infarction: No additional benefit from immediate percutaneous coronary angioplasty. Lancet 1988; 1: 197-203.

14. Harrison JK, Califf RM, Harrelson-Woodlief L, Kereiakes D, George BS, Stack RS, Ellis SG, Lee KL, O'Neill W, Topol EJ and the TAMI Study Group. Systolic left ventricular function after reperfusion therapy for acute myocardial infarction: An analysis of determinants of improvement. Circulation 1531-1541, 1993.)

15. Arnold AER, Simoons ML, Van de Werf F, et al. Recombinant tissue-type plasminogen activator and immediate angioplasty in acute myocardial infarction. One -year follow-up. Circulation 1992; 86: 111-20.

16. Waller BF, Rothbaum DA, Pinkerton CA, et al. Status of the myocardium and infarct related coronary artery in 19 necropsy patients with acute recanalization using pharmacologic (streptokinase, r-tissue plasminogen activator), mechanical (percutaneous transluminal coronary angioplasty) or combined types of reperfusion therapy. J Am Coll Cardiol 1987; 9: 785-92.

17. Duber C, Jungbluth A, Rumpelt HJ, et al. Morphology of the coronary arteries after combined thrombolysis and percutaneous coronary angioplasty for acute myocardial infarction. Am J Cardiol 1986; 58: 698-703.

18. SWIFT Trial Study Group. SWIFT trial of delayed elective intervention v. conservative treatment after thrombolysis with anistreplase in acute myocardial infarction. Br Med J 1991; 302: 555-60.

19. The TIMI Study Group. Comparison of invasive and conservative strategies after treatment with intravenous tissue plasminogen activator in acute myocardial infarction. Results of the TIMI phase II trial. N Engl J Med 1989; 320: 618-27.

20. Williams DO, Braunwald E, Knatterud G, et al. One-year results of the TIMI phase II trial. Circulation 1992; 85: 533-42.

21. Terrin ML, Williams DO, Kleiman NS, Willerson JT, Mueller HS, Desvigne-Nickens P, Forman SA, Knatterud GL, Braunwald E, for the TIMI II Investigators. Two- and three-year results of the thrombolysis in myocardial infarction (TIMI) phase II clinical trial. J Am Coll Cardiol 1993; 22:1763016722.]

22. Barbash GI, Roth A, Hod H, et al. Randomized controlled trial of late in-hospital angiography and angioplasty versus conservative management after treatment with recombinant tissue-type plasminogen activator in acute myocardial infarction. Am J Cardiol 1990; 66: 538-45.

23. Ellis SG, Mooney MR, George BS, et al. Randomized trial of late elective angioplasty versus conservative management for patients with residual stenosis after thrombolytic treatment of myocardial infarction. Circulation 1992; 86: 1400-6.

24. Baim DS, Diver DJ, Feit F, et al. Coronary angioplasty within the Thrombolysis in Myocardial Infarction II study. Circulation 1992; 85: 95-105.

25. Chesebro JH, Knatterud G, Roberts R, et al. Thrombolysis in Myocardial Infarction Trial, phase I: A comparison between intravenous tissue plasminogen activator and intravenous streptokinase - clinical findings through hospital discharge. Circulation 1987; 76: 142-54.

26. Neuhaus KL, Von Essen R, Tebbe U, et al. Improved thrombolysis in acute myocardial infarction with front-loaded administration of altepase: Results of the rt-PA-APSAC patency study (TAPS). J Am Coll Cardiol 1992; 19: 885-91.

27. Califf RM, Topol EJ, George BS, et al. Characteristics and outcome of patients in whom reperfusion with intravenous tissue plasminogen activator fails: Results of the TAMI I trial. Circulation 1988; 77: 1090-9.

28. Abbotsmith CW, Topol EJ, George BS, et al. Fate of patients with patency of the infarct related vessel achieved with successful thrombolysis versus rescue angioplasty. J Am Coll Cardiol 1990; 16: 770-8.

29. Lange RA, Cigarroa RG, Hillis LD. Influence of residual antegrade coronary blood flow on survival after myocardial infarction in patients with multivessel coronary artery disease. Coronary Artery Dis 1990; 1: 59-63.

30. Cigarroa RG, Lange RA, Hillis LD. Prognosis after acute myocardial infarction in patients with and without residual anterograde coronary blood flow. Am J Cardiol 1989; 64: 155-60.

31. Kennedy JW, Ritchie JL, Davis KB, Fritz JK. Western Washington randomized trial of intracoronary streptokinase in acute myocardial infarction. N Engl J Med 1983; 309: 1477-82.

32. Califf RM, O'Neill WW, Stack RS, et al. Failure of simple clinical measurements to predict perfusion status after intravenous thrombolysis. Ann Intern Med 1988; 108: 658-62.

33. Krucoff MW, Wagner NB, Pope JE, et al. The portable programmable microprocessor-driven real-time 12 lead electrocardiographic monitor: A preliminary report of a new device for the noninvasive detection of successful reperfusion or silent coronary reocclusion. Am J Cardiol 1990; 65: 143-8.

34. Ellis AK, Little T, Masud ARZ, et al. Early noninvasive detection of successful reperfusion in patients with acute myocardial infarction. Circulation 1988; 78: 1352-7.

35. Reimer KA, Lowe JE, Rasmussen MM, Jennings RB. The wave front phenomenon of ischemic cell death. Circulation 1977; 56: 786-94.

36. Ellis SE, O'Neill WW, Bates R, et al. Implications for triage from survival and left ventricular functional recovery analyses in 500 patients treated with coronary angioplasty for acute myocardial infarction. J Am Coll Cardiol 1989; 13: 1251-9.

37. Lee L, Bates ER, Pitt B, Walton, et al. Percutaneous coronary angioplasty improves survival in acute myocardial infarction complicated by cardiogenic shock. Circulation 1988; 78: 1345-51.

38. Lee L, Erbel R, Brown TM, Laufer N, et al. Multicenter registry of angioplasty therapy of cardiogenic shock: Initial and long-term survival. J Am Coll Cardiol 1991; 17: 599-603.

39. Moosvi AR, Khafa F, Villanueva L, et al. Early revascularization improves survival in cardiogenic shock complicating acute myocardial infarction. J Am Coll Cardiol 1992; 19: 907-14.

40. Gacioch GM, Ellis SG, Lee L, et al. Cardiogenic shock complicating acute myocardial infarction: The use of coronary angioplasty and the integration of the new support devices into patient management. J Am Coll Cardiol 1992; 19: 647-53.

41. Hibbard MD, Holmes DR, Bailey KR, et al. Percutaneous transluminal coronary angioplasty in patients with cardiogenic shock. J Am Coll Cardiol 1992; 19: 639-46.

42. Bates ER, Topol EJ. Limitations of thrombolytic therapy for acute myocardial infarction complicated by congestive heart failure and cardiogenic shock. J Am Coll Cardiol 1991; 18: 1077-84.

43. Stadius ML, Davis K, Maynard C, et al. Risk stratification for one year survival based on characteristics identified in the early hours of acute myocardial infarction. Circulation 1986; 74: 703-11.

44. Dalen JE, Gore JM, Braunwald E, and the TIMI Investigators. Six and twelve month follow-up of the phase I Thrombolysis in Myocardial Infarction (TIMI) trial. Am J Cardiol 1988; 62: 179-85.

45. Ohman EM, Califf RM, Topol EJ, et al. Characteristics and importance of reocclusion following successful reperfusion therapy in acute myocardial infarction. Circulation 1990: 82: 781-91.

46. Jeremy RW, Hackworthy RA, Bautovich G, et al. Infarct artery perfusion and changes in left ventricular volume in the month after acute myocardial infarction. J Am Coll Cardiol 1987; 9: 989-95.

47. Kersschot IE, Brugada P, Ramentol M, et al. Effects of early reperfusion in acute myocardial infarction on arrhythmias induced by programmed stimulation: A prospective, randomized study. J Am Coll Cardiol 1986; 7: 1234-42.

48. Braunwald E. Myocardial reperfusion, limitation of infarct size, reduction of left ventricular dysfunction, and improved survival. Should the paradigm be expanded? Circulation 1989; 79: 441-4.

49. Topol EJ, Califf RM, Vandormael M, et al. A randomized trial of late reperfusion therapy for acute myocardial infarction. Circulation 1992; 85: 2090-9.

50. Ellis SG, Van de Werf F, Ribeiro-daSilva E, Topol EJ. Present status of rescue coronary angioplasty: Current polarization of opinion and randomized trials. J Am Coll Cardiol 1992; 19: 681-6.

51. Hartzler GO, Rutherford BD, McConahay DR, et al. Percutaneous transluminal coronary angioplasty with and without thrombolytic therapy for treatment of acute myocardial infarction. Am Heart J 1983; 106: 965-73.

52. Meier B. Balloon angioplasty for acute myocardial infarction. Was it buried alive? Circulation 1990; 82: 2243-5.

53. Brundage BH. Because we can, should we? J Am Coll Cardiol 1990; 15: 544-5.

54. Flaker GC, Webel RR, Meinhardt S, Anderson S, Santolin C, Artis, et al. Emergency angioplasty in acute anterior myocardial infarction. Am Heart J 1989; 118:1154-60.

55. Marco J, Caster L, Szatmary LJ, Fajadet J. Emergency percutaneous transluminal coronary angioplasty without thrombolysis as initial therapy in acute myocardial infarction. Int J Cardiol 1987; 15:55-63.

56. Ellis SG, O'Neill WW, Bates ER, Walton JA JR, Nabel EG, Werns SW, et al. Implications for patient triage from survival and left ventricular functional recovery analyses in 500 patients treated wtih coronary angioplasty for acute myocardial infarction. J Am Coll Cardiol 1989; 13:1251-9.

57. Rothbaum DA, Linnemeier TJ, Landin RJ, Steinmetz EF, Hillis JS, Hallam CC, et al. Emergency percutaneous transluminal coronary angioplasty in acute myocardial infarction: A 3 year experience. J Am Coll Cardiol 1987; 10:264-72.

58. Brodie BR, Weintraub RA, Stuckey TD, LeBauer EJ, Katz JD, Kelly TA, et al. Outcomes of direct coronary angioplasty for acute myocardial infarction in candidates and non-candidates for thrombolytic therapy. Am J Cardiol 1991; 67:7-12.

59. Bittl JA. Indications, timing, and optimal technique for diagnostic angiography and angioplasty in acute myocardial infarction. Chest 1991; 99:150S-6S.

60. Kahn JK, O'Keefe JH JR, Rutherford BD, McConahay DR, Johnson WL JR, Giorgi LV, et al. Timing and mechanism of in-hospital and late death after primary coronary angioplasty during acute myocardial infarction. Am J Cardiol 1990; 66:1045-8.

61. Beauchamp GD, Vacek JL, Robuck W. Management comparison for acute myocardial infarction: Direct angioplasty versus sequential thrombolysis angioplasty. Am Heart J 1990; 120:237-42.

62. Grines CK, Meany TB, Weintraub R, Strzelecji M, Cragg DR, Timmis GC, et al. Streptokinase angioplasty myocardial infarction trial: Early and late results [abstr] J Am Coll Cardiol 1991; 17:336A.

63. Williams DO, Holubkov AL, Detre KM, Hommes DR, Kent KM. Impact of pretreatment by thrombolytic therapy upon outcome of emergent direct coronary angioplasty for patients with acute myocardial infarction [abstr] J Am Coll Cardiol 1991; 17:337A.

64. O'Keefe JH, Rutherford BD, McConahay DR, et al. Early and late results of coronary angioplasty without antecedent thrombolytic therapy for acute myocardial infarction. Am J Cardiol 1989; 64: 1221-30.

65. O'Keefe JH, Rutherford BD, McConahay DR, et al. Myocardial salvage with direct coronary angioplasty for acute infarction. Am Heart J 1992; 123: 1-6.

66. Stone GW, Rutherford BD, McConahay DR, et al. Direct coronary angioplasty in acute myocardial infarction: Outcome in patients with single vessel disease. J Am Coll Cardiol 1990; 15: 534-43.

67. Kander NH, O'Neill WW, Topol EJ, et al. Long-term follow-up of patients treated with coronary angioplasty for acute myocardial infarction. Am Heart J 1989; 118: 228-33.

68. Ellis SG, Topol EJ, Gallison L, et al. Predictors of success for coronary angioplasty performed for acute myocardial infarction. J Am Coll Cardiol 1988; 12: 1407-15.

69. Kahn JK, Rutherford BD, McConahay DR, et al. Catheterization laboratory events and hospital outcome with direct angioplasty for acute myocardial infarction. Circulation 1990; 82: 1910-5.

70. Gacioch GM, Topol EJ. Sudden paradoxic clinical deterioration during angioplasty of the occluded right coronary artery in acute myocardial infarction. J Am Coll Cardiol 1989; 14: 1202-9.