REVIEW

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Primary percutaneous coronary intervention for acute MI: Improving access and outcomes

ABSTRACT

Patients with acute myocardial infarction (MI) with ST-segment elevation have better outcomes with primary percutaneous coronary intervention (PCI) than with fibrinolytic therapy. Multiple clinical trials in the past 10 years have addressed ways to improve PCI as primary therapy for acute MI. Logistic strategies to improve access to PCI are being studied.

KEY POINTS

Abciximab, a platelet inhibitor, reduces the incidence of adverse outcomes when given before primary PCI without increasing the bleeding risk unacceptably; data with other agents of this class are not as robust.

Stents reduce the incidence of restenosis after primary PCI. Whether drug-eluting stents will be more beneficial remains to be determined.

Pending data from studies of low-molecular-weight heparin in primary PCI, unfractionated heparin is still the standard of care.

The best therapy for patients who enter the medical system in hospitals that cannot perform primary PCI remains to be elucidated. A possibility is "facilitated PCI," ie, fibrinolytic therapy followed immediately by PCI.

WE HAVE KNOWN for some time that patients have a better chance of surviving acute myocardial infarction (MI) with ST-segment elevation and of not having another MI or other adverse outcome if they are treated with percutaneous coronary intervention (PCI) rather than with fibrinolytic therapy.

But adverse outcomes still occur with PCI. Accordingly, clinical researchers have been working to improve PCI, including therapies to decrease myocardial injury and improve microcirculatory function after reperfusion. Also, logistical strategies to improve access to PCI are under investigation. This article discusses:

- Use of adjunctive antiplatelet treatment
- The role of stenting, including new drug-eluting stents to prevent restenosis
- Whether low-molecular-weight heparins are better than standard heparin
- How to minimize delay from symptom onset to reperfusion, including "facilitated PCI" (fibrinolytic therapy plus PCI), primary PCI in community hospitals, and improving transfer times.

TERMS

PCI includes balloon angioplasty, stent implantation, and various techniques of plaque modification and thrombus aspiration. *Primary PCI*, ie, the use of PCI as the first-line therapy for acute MI, should be distinguished from *rescue PCI*, which is performed after it is clinically evident that fibrinolytic therapy has failed, and from *facilitated PCI*, which is a

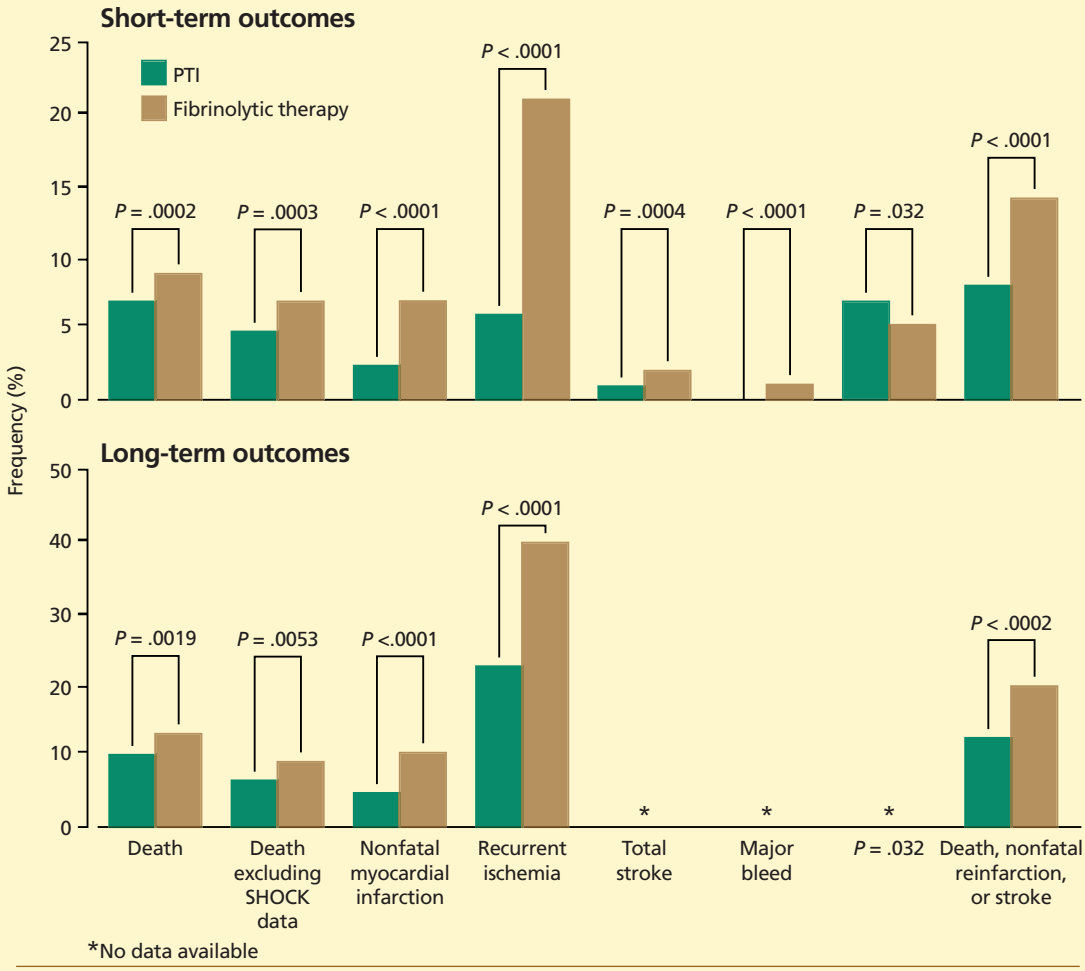

FIGURE 1. Short-term and long-term clinical outcomes in patients who underwent primary percutaneous coronary intervention (PCI) or fibrinolytic therapy for acute myocardial infarction (MI) in 23 randomized trials.

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Short-term mortality in acute MI: 7.0% with angioplasty vs 9.3% with fibrinolysis

strategy of PCI immediately following (and irrespective of the results of) pharmacologic reperfusion therapy. This therapy frequently uses lower doses of fibrinolytic agents in conjunction with potent platelet inhibitors.

EVOLUTION OF ACUTE MI CARE

The guiding principle in managing acute ST-elevation MI is that patients are less likely to die if they achieve early, complete, and sustained reperfusion. This "time-dependent open-artery hypothesis" was confirmed in trials of fibrinolytic therapy that showed an association between patency of the culprit coronary artery and favorable clinical outcomes.[1,2]

Several large randomized trials established that more patients survive an acute MI if they receive fibrinolytic therapy than if they receive conservative management.[3–5]

At first, PCI was used as a supplement to fibrinolysis in a delayed and selective manner. In fact, a number of randomized prospective trials[6–8] showed that routinely performing angioplasty immediately after intravenous fibrinolysis was not superior to the strategy of

TABLE 1

fibrinolysis alone with deferred angioplasty.

A pharmacologic approach to managing acute ST-elevation MI has several advantages. Fibrinolytic agents are widely and rapidly available. The "learning curve" in using them is not steep, and they are suitable for patients whose coronary anatomy would preclude PCI. On the other hand, major limitations of fibrinolysis include an increased incidence of hemorrhagic stroke and a limited rate of durable reperfusion (50%–60%).

Prompted by favorable observational data on primary angioplasty,[9–32] several randomized prospective trials[33] compared fibrinolysis and primary angioplasty as separate reperfusion strategies and showed that fewer patients who underwent primary angioplasty reached the composite end point of death, recurrent MI, or intracranial hemorrhage.

Keeley et al[34] performed a meta-analysis of 23 prospective randomized trials comparing primary PCI with fibrinolysis in 7,739 patients with acute MI. Clinical outcomes were better with primary PCI than with fibrinolysis (FIGURE 1). The short-term mortality rate was 7.0% with PCI compared with 9.3% with fibrinolysis, a 27% relative risk reduction (P = .0002). Rates of stroke and nonfatal reinfarction were also lower with angioplasty. The mortality rate continued to be lower after PCI in long-term follow-up.

The recent American College of Cardiology/American Heart Association (ACC/AHA) guidelines for management of patients with ST-elevation MI stress the importance of reducing the time from symptom onset to reperfusion therapy and providing aggressive risk modification after the initial hospitalization.[35] The summary for the choice of the reperfusion therapy is shown in TABLE 1.

Primary PCI has recently been improved with pharmacological and mechanical innovations, such as the platelet glycoprotein (GP) IIb/IIIa receptor inhibitors and stents.

GLYCOPROTEIN IIB/IIIA INHIBITION IMPROVES OUTCOMES IN PCI

GP IIb/IIIa receptor blockers—powerful drugs that inhibit platelet aggregation—have been studied extensively in PCI. For primary PCI, most of the experience has been with abciximab, a monoclonal antibody against the platelet GP IIb/IIIa receptor.

Randomized trials of abciximab

Topol et al[36] pooled five trials (see below) and found that the 30-day incidence of the combined end point of death, reinfarction, or target-vessel revascularization procedure was 4.8% with abciximab vs 8.8% with placebo

(odds ratio 0.54, $P < .05$; FIGURE 2). The benefit persisted at 6 months.

RAPPORT (the ReoPro and Primary PTCA Organization and Randomized Trial)[37] included 483 patients undergoing primary balloon angioplasty who were randomized to receive either adjunctive abciximab or placebo.

Abciximab offered no significant benefit in the prespecified primary end point of the study, the 6-month incidence of death, recurrent MI, or any target-vessel revascularization. However, at 30 days, the incidence of the combined end point of death, reinfarction, or *urgent* target-vessel revascularization was 5.8% in the abciximab group vs 11.2% in the placebo group ($P = .03$). Major bleeding was increased in the abciximab group, likely because a high dose of heparin was used in this blinded study.

ISAR-2 (the second Intracoronary Stenting and Antithrombotic Regimen trial)[38] included 401 patients who underwent stenting within 48 hours after the onset of acute MI and were randomized to receive either abciximab or placebo.

The abciximab group had a significantly lower rate of the 30-day composite end point of death, reinfarction, and target-vessel revascularization (5.0% vs 10.5%, $P = .038$).

This trial differs from the others in the meta-analysis[36] in that it included patients in whom PCI was performed as late as 48 hours after the onset of MI.

ADMIRAL (the Abciximab Before Direct Angioplasty and Stenting in Myocardial Infarction Regarding Acute and Long-Term Follow-up trial)[39] randomized 300 patients with acute MI to receive either adjunctive abciximab or placebo. The study drug was given immediately after randomization and in all cases before the angioplasty sheath was inserted.

More patients who received abciximab achieved complete reperfusion (grade 3 flow on the TIMI scale). Immediately before PCI, the rates were 16.8% with abciximab vs 5.4% with placebo ($P = .01$); immediately after PCI, the rates were 95.1% vs 86.7% ($P = .04$).

At 30 days, 6.0% of the abciximab group had suffered the primary composite end point of death, reinfarction, or urgent target-vessel revascularization, vs 14.6% with placebo ($P = .01$). At 6 months the rates were 7.4% with abciximab vs 15.9% with placebo ($P = .02$). In contrast to the RAPPORT trial, there was no excess major bleeding with abciximab (0.7% vs 0.0%).

ACE (the Abciximab and Carbostent Evaluation trial)[40] randomized 400 patients undergoing primary PCI to receive either adjunctive abciximab or placebo.

With abciximab, infarcts were smaller (as measured by nuclear scintigraphy), ST-segment elevation resolved sooner, and the 30-day incidence of the primary composite end point of death, reinfarction, target-vessel revascularization, or stroke was lower (4.5% vs 10.5%, $P = .023$). At 6 months, the incidence of the composite end point of death or reinfarction was 5.5% in the abciximab group vs 13.5% in the placebo group ($P = .011$). At 1

In PCI for acute MI, abciximab is better than placebo

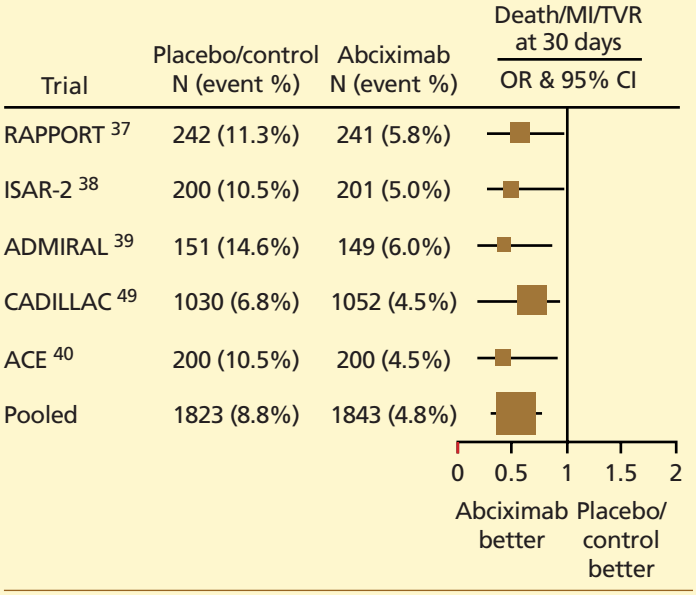

FIGURE 2. Rates of death, reinfarction, and target-vessel revascularization (TVR) procedure at 30 days in five trials comparing adjunctive abciximab and placebo during percutaneous coronary intervention (PCI) for acute myocardial infarction (MI). Two trials (ACE, CADILLAC) included stroke in the composite end point, but the incidence was quite low.

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year, 5% of the abciximab-treated patients had died compared with 12% of those who received placebo ($P = .017$).[41]

STOPAMI (the Stent Versus Thrombolysis for Occluded Coronary Arteries in Patients with Acute Myocardial Infarction trial)[42] revealed that, in 140 patients with acute MI, those who underwent PCI with stenting and abciximab had smaller infarcts and better clinical outcomes at 6 months compared with those who received alteplase (tissue-plasminogen activator, t-PA) in an accelerated ("front-loaded") regimen.

The median infarct size in the PCI group was 14.3% of the left ventricle compared with 19.4% in the fibrinolytic therapy group ($P = .02$). The incidence of the secondary composite end point of death, reinfarction, or stroke at 6 months was 8.5% with PCI vs 23.2% with fibrinolysis ($P = .02$).

Data from studies using other GP IIb/IIIa inhibitors (On-TIME [tirofiban], INAMI [eptifibatide]) are more equivocal and much less supportive of definitive recommendations. The ACC/AHA guidelines[35] give these other agents a class IIB recommendation (the benefit is at least as great as the risk but additional studies with broad objectives are needed; the treatment *may* be considered).

Abciximab: bottom line. Using abciximab as early as possible after diagnosis carries a class IIa recommendation (the benefit exceeds the risk; additional studies with focused objectives are needed; *it is reasonable* to give the treatment).[35] I recommend it strongly.

Abciximab reduced adverse outcomes in multiple trials of primary PCI

STENTING REDUCES RESTENOSIS

Patients who undergo elective PCI have a lower rate of restenosis afterwards if they receive a stent.[43,44] Moreover, observational studies documented the feasibility of stenting during primary angioplasty,[45–47] setting the stage for randomized trials in this setting.

Randomized trials of stenting in acute MI

PAMI Stent (the Stent Primary Angioplasty in Myocardial Infarction randomized trial)[48] compared stenting (using the heparin-coated Palmaz-Schatz stent) and balloon angioplasty in 900 patients with acute MI.

Six months after the procedure, patients who received stents had greater luminal diameters and a lower incidence of restenosis (20.3% vs 33.5%, $P < .001$). The 6-month incidence of the primary clinical composite end point of death, reinfarction, disabling stroke, or ischemia-driven target-vessel revascularization was 12.6% in the stent group vs 20.1% in the balloon angioplasty group ($P < .01$), but the entire difference was due to less need for revascularization.

CADILLAC (the Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications trial)[49] compared four treatments in a two-by-two factorial design: balloon angioplasty alone, balloon angioplasty with abciximab, stenting alone, and stenting with abciximab.

The incidence of the primary end point—death, reinfarction, disabling stroke, or ischemia-driven target-vessel revascularization at 6 months—was 20.0% with balloon angioplasty alone, 16.5% with balloon angioplasty plus abciximab, 11.5% with stenting alone, and 10.2% with stenting plus abciximab ($P = .03$ for stenting alone vs balloon angioplasty plus abciximab), but the difference was due entirely to fewer ischemia-driven revascularizations of the culprit artery.

The risk of subacute thrombosis of an infarct-related artery by 30 days was significantly lower with abciximab than with placebo (0.4% vs 1.4%, $P < .001$). However, more abciximab recipients needed blood transfusions or developed thrombocytopenia.

Of note, the mortality rate was significantly lower in the CADILLAC trial than in other ST-elevation MI trials. This may have been in part because the patients were at lower risk to begin with, and they were randomized after undergoing angiography and after being determined to be suitable for stenting.

Drug-eluting stents

Although yet to be evaluated in a large randomized trial, the use of sirolimus-eluting stents in acute ST-elevation MI has thus far not been associated with an increase in acute stent thrombosis. Several hundred thousand patients have received these stents, but it remains to be proven whether the risk of acute

stent thrombosis is different from that with bare metal stents. One small trial found a rate of acute stent thrombosis similar to that with bare metal stents.[50]

The RESEARCH (Rapamycin-eluting Stent Evaluated at Rotterdam Cardiology Hospital) registry[51] collected data on 89 primary PCI procedures in Rotterdam, Netherlands. At a mean follow-up of 218 days, 1 patient had died; there had been no MIs and no repeat interventions. Notably, there were no cases of stent thrombosis or angiographic restenosis.

Lemos et al[52] compared outcomes in 186 patients who underwent primary PCI with sirolimus-eluting stents and in 183 historical controls who received bare metal stents. There were no cases of stent thrombosis with sirolimus-coated stents, and at 300 days the incidence of the combined adverse-event end point was lower in the sirolimus group, mainly due to fewer repeat interventions.

Bottom line. Until these findings are proven in a larger number of patients, sirolimus-coated stents should be used with caution in primary PCI. As yet there are no data with paclitaxel-coated stents in this situation.

So far, the risk of acute stent thrombosis does not seem higher with sirolimus stents

FACILITATED PCI: FIBRINOLYSIS, THEN PCI

Combining fibrinolysis and primary PCI makes theoretical sense, as early reperfusion would be coupled with percutaneous or surgical revascularization. This approach has been termed "facilitated PCI."

Dudek et al[53] examined this strategy in 200 acute MI patients in Poland being transferred to a tertiary referral center. The patients received reduced-dose alteplase plus abciximab and then underwent immediate PCI. The 30-day mortality rate in this prospective registry was quite low at 3.5%.

PACT (the Plasminogen-activator Angioplasty Compatibility Trial)[54] randomized 606 patients with acute ST-elevation MI to receive alteplase 50 mg or placebo. Both groups then underwent angiography (the mean time from study drug administration to angiography was 49 minutes), and if the flow in the infarct-related artery was not optimal, angioplasty was performed. There was no difference in ventricular function or adverse clinical end points between the study groups.

In **SPEED** (the Strategies for Patency Enhancement in the Emergency Department trial)[55] patients received fibrinolytic therapy (either half-dose reteplase plus abciximab or full-dose reteplase alone); then early PCI was encouraged. Patients who underwent facilitated PCI had fewer ischemic events and bleeding complications than did patients not undergoing early PCI.

GRACIA-2 (the second *Grupo de Análisis de la Cardiopatía Isquémica Aguda* trial) randomized 212 patients with acute ST-elevation MI either to undergo primary PCI immediately or to receive tenecteplase and immediately afterward undergo PCI.

More patients who underwent facilitated PCI achieved complete resolution of ST-elevation at 6 hours; clinical outcomes were similar between the two strategies. Results were presented at the Congress of the European Society of Cardiology, August 30 to September 3, 2003, Vienna, Austria.

BRAVE (the Bavarian Reperfusion Alternatives Evaluation trial)[56] randomized 253 patients with ST-elevation MI to receive either half-dose reteplase plus abciximab or abciximab only, after which both groups underwent angiography and PCI, when indicated. There was no significant difference between the two groups in infarct size or ischemic complications. However, there were more bleeding complications in the reteplase group.

CAPITAL AMI (the Combined Angioplasty and Pharmacological Intervention Versus Thrombolytics Alone in Acute Myocardial Infarction trial) randomized 170 patients with ST-elevation MI to either receive tenecteplase only or to receive tenecteplase and then be transferred for PCI.

At 30 days the tenecteplase-plus-PCI group had a lower incidence of the primary composite end point of death, reinfarction, unstable ischemia, and stroke. Results were presented by Michel R. LeMay, MD, at the American College of Cardiology Scientific Sessions, March 7 to 10, 2004, New Orleans, LA.

Bottom line. Further studies are required to evaluate the strategy of facilitated PCI.

ARE LOW-MOLECULAR-WEIGHT HEPARINS BETTER?

For decades, antithrombin therapy with intravenous unfractionated heparin has been a mainstay of adjunctive medical therapy for acute ST-elevation MI. Recently, low-molecular-weight heparins have been evaluated in acute ischemic syndromes.

ASSENT-3 (the third Assessment of the Safety and Efficacy of a New Thrombolytic Regimen randomized trial)[57] compared enoxaparin and unfractionated heparin as an adjunct to fibrinolytic therapy for acute ST-elevation MI. Enoxaparin recipients had a lower incidence of the primary end point of death within 30 days, in-hospital reinfarction, or in-hospital refractory ischemia (11.4% vs 15.4%, relative risk 0.74, P = .0002). Bleeding complications were similar in the two groups.

Bottom line. Until data from studies of enoxaparin in primary PCI are available, intravenous unfractionated heparin remains the standard of care for antithrombin therapy during mechanical reperfusion of ST-elevation MI. Enoxaparin should be used cautiously in patients older than 75 years receiving fibrinolytic therapy, given the increased stroke risk.[58]

LOGISTIC CONSIDERATIONS

Decreasing delay in primary PCI

The key challenge with primary PCI is to minimize the delay from symptom onset to reperfusion. This interval encompasses the time from symptom onset to medical contact and the subsequent time to reperfusion (the "door-to-balloon" time).

The Second National Registry of Myocardial Infarction demonstrated a direct correlation between the door-to-balloon time and the in-hospital mortality rate.[59] Similarly, the Global Use of Strategies To Open Occluded Coronary Arteries in Acute Coronary Syndromes IIb **(GUSTO IIb)** trial demonstrated that longer enrollment-to-balloon times were associated with higher 30-day mortality rates.[60]

De Luca et al[61] showed that in primary PCI, the symptom onset-to-balloon time, but not the door-to-balloon time correlates with the mortality rate at 1 year. The same group also found that the mortality rate at 1 year increases with each 30-minute increment in ischemic time.[62] These findings highlight the importance of the total ischemic time as a predictor of myocardial damage and death.

CAPTIM (the Comparison of Angioplasty and Prehospital Thrombolysis in Acute Myocardial Infarction)[63] and the **ASSENT-3 PLUS**[58] trial examined the safety and efficacy of starting fibrinolytic therapy before the patient reaches the hospital. In well-developed health care systems this is an acceptable strategy.

Although public education may decrease the time from symptom onset to hospitalization, more effort is invested in reducing the door-to-balloon time.

Primary PCI in community hospitals

Traditionally, primary PCI was done only at hospitals equipped for on-site cardiac surgery. However, with stenting, the need for emergency coronary artery bypass grafting has decreased dramatically.[64]

C-PORT (the Cardiovascular Patient Outcomes Research Team trial)[65] tested whether primary PCI can be done in hospitals that do not perform coronary artery bypass grafting. Between 1996 and 1999, 451 patients presented with acute ST-elevation MI at 11 community hospitals and were randomized to undergo either fibrinolytic therapy with front-loaded t-PA or primary PCI.

The 6-month incidence of the primary end point of death, reinfarction, or stroke was 12.4% with primary PCI vs 19.9% with t-PA (P = .03), showing the feasibility of performing primary PCI in community hospitals without cardiac surgery backup.

Public education may decrease the symptom onset-to-hospital time

Transferring patients for primary PCI

DANAMI-2 (the second Danish Multicenter Randomized Study on Fibrinolytic Therapy Versus Acute Coronary Angioplasty in Acute Myocardial Infarction)[66] evaluated the strategy of transferring ST-elevation MI patients to another hospital to undergo primary PCI. The transfer distance was up to 95 miles (mean 35 miles), and the transfer time was less than 3 hours (median 67 minutes).

A total of 1,562 patients were randomized at community and tertiary hospitals to either be transferred for primary PCI (or to undergo it on-site if the hospital had a catheterization laboratory) or to receive fibrinolytic therapy (alteplase 100 mg in a front-loaded regimen). The primary end point was the 30-day incidence of death, reinfarction, or stroke.

The study was stopped early because of a large reduction in reinfarction with the PCI strategy; the incidence was 1.6% with PCI vs 6.3% with fibrinolysis ($P < .0001$). This resulted in a 45% relative risk reduction in the primary combined end point (8% vs 14%, $P = .0003$), but there was no difference in death or stroke. The time from randomization to treatment was 90 minutes in the PCI group vs 20 minutes in the fibrinolysis group.

Notably, the rate of rescue or adjunctive PCI was much lower in the DANAMI 2 trial (2.5%) than in other fibrinolytic trials,[57,67,68] which had rates of about 7% to 11%. Rates of reinfarction were also lower in these contemporary fibrinolytic trials (1.8% to 4.2% vs 6.3% in the DANAMI 2 trial).

Unfortunately, interhospital transfer in the United States is much slower than in DANAMI 2, limiting the practical application of these results.

PRAGUE-2 (the second Primary Angioplasty in Acute Myocardial Infarction Patients From General Community Hospitals Transported for Percutaneous Transluminal Coronary Angioplasty Units Versus Emergency Thrombolysis trial)[69] randomized patients with ST-elevation MI and symptoms of less than 12 hours to undergo either on-site fibrinolysis or transfer to a primary PCI center.

The mortality rate was lower with primary PCI, but the difference was not statistically significant. Further analysis showed no mortality benefit in patients presenting within 3 hours from symptom onset, but did show a significant mortality reduction (6% vs 15%) in patients presenting at 3 to 12 hours who were transferred to receive primary PCI.

Air PAMI (the Air Primary Angioplasty in Myocardial Infarction trial)[70] examined the optimal reperfusion strategy for patients presenting with acute ST-elevation MI to hospitals without a cardiac catheterization laboratory.

For the 138 high-risk patients randomized, the 30-day rate of major adverse cardiac events was lower among those transferred for primary angioplasty than in those who received on-site fibrinolytic therapy (8.4% vs 13.6%). This difference did not reach statistical significance, as the study was underpowered due to recruiting difficulties.

Of note, the randomization-to-treatment time was only 155 minutes in the transfer group vs 51 minutes in the fibrinolytic therapy group.

CAPTIM[63] compared the strategies of prehospital fibrinolysis and primary PCI. Patients (n = 840) presenting within 6 hours of symptom onset with acute ST-elevation MI were randomized to either receive prehospital alteplase or be transferred to undergo PCI. The time from symptom onset until the start of therapy was 130 minutes for fibrinolysis and 190 minutes for PCI.

The groups did not differ significantly in the 30-day incidence of the primary composite end point of death, reinfarction, or disabling stroke (6.2% for angioplasty vs 8.2% for fibrinolytic therapy, $P = .29$). The study was stopped early due to inadequate funding and was therefore likely underpowered.

In this group of patients treated relatively early after MI onset, however, more patients died in the PCI group (4.8% vs 3.8%, $P = .62$), mostly because more PCI patients developed cardiogenic shock (4.9% vs 2.5%, $P = .09$). Also of note, 26% of the patients in the fibrinolytic therapy group underwent immediate rescue PCI, a much higher rate than in other contemporary fibrinolytic trials.

The key challenge with primary PCI is to minimize delay

Dalby et al[71] performed a meta-analysis of trials[63,66,69,70,72,73] comparing transfer for primary PCI vs fibrinolytic therapy (**FIGURE 3**). Of note, the three largest trials (DANAMI-2,[66] PRAGUE-2,[69] and CAPTIM[63]) accounted for 83% of the statistical weight. The mean time to PCI in the transfer groups was between 80 and 122 minutes.

The incidence of reinfarction was lower among patients transferred for primary PCI than among patients who received fibrinolytic therapy (relative risk 0.32, $P < .001$), as was the incidence of stroke (relative risk 0.44, $P = .015$). There was a trend of reduced mortality among the PCI group (relative risk 0.81, $P = .08$). Interestingly, if the CAPTIM trial was

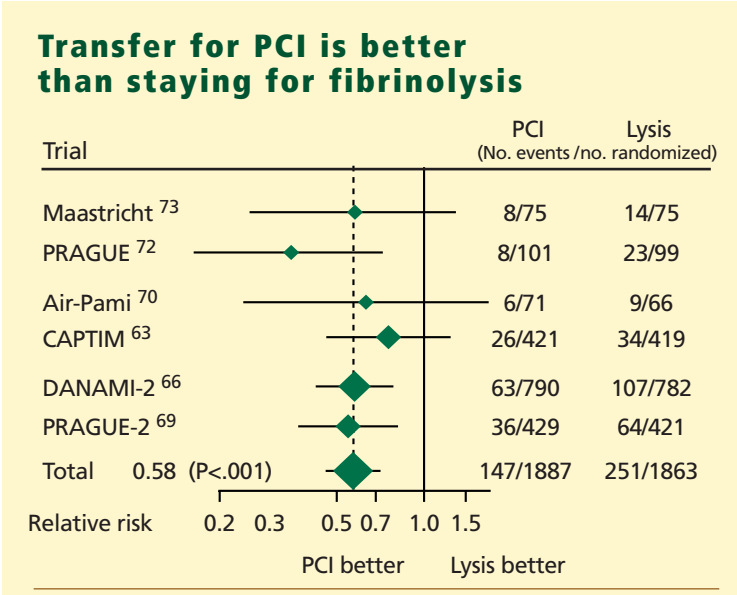

FIGURE 3. Relative risk for the composite of death, reinfarction, and stroke with thrombolysis and transfer for primary PCI in six trials.

REPRODUCED WITH PERMISSION FROM DALBY M, BOUZAMONDO A, LECHAT P, MONTALESCOT G. TRANSFER FOR PRIMARY ANGIOPLASTY VERSUS IMMEDIATE THROMBOLYSIS IN ACUTE MYOCARDIAL INFARCTION. A META-ANALYSIS. CIRCULATION 2003; 108:1809–1814.

excluded, leaving only trials in which patients were treated in hospitals, transfer for PCI was associated with a lower mortality rate compared with fibrinolytic therapy (relative risk 0.76, $P = .035$).

Nallamothu and Bates,[74] in a meta-analysis of trials comparing primary PCI and fibrinolysis, discovered that the mortality benefit with primary PCI may be lost if the door-to-balloon time is more than 1 hour longer than the door-to-needle time for fibrin-specific fibrinolytic therapy. In their analysis, the two reperfusion strategies became equivalent with regard to mortality after a PCI-related time delay of 62 minutes.

Guidelines from the ACC/AHA[35] call for transfer for PCI in patients presenting more than 3 hours from MI onset if the first balloon inflation would occur within 60 minutes of when the fibrinolytic agent could be infused. If presentation is within 3 hours of symptom onset, the two strategies are equivalent, as long as PCI can be performed within 90 minutes of arrival.

Cardiogenic shock

Patients who present in cardiogenic shock are at the highest risk of all patients with acute MI. An aggressive strategy of early revascularization and also inserting an intra-aortic balloon pump is the standard of care.

Prospective data from the Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) trial, and observational data from the GUSTO-1 trial,[75] support primary PCI or early bypass grafting as the strategies of choice.[76]

FUTURE DIRECTIONS

Recently, the Enhanced Myocardial Efficacy and Recovery by Aspiration of Liberalized Debris (EMERALD) trial found that infarcts were no smaller if the PercuSurge emboli protection device was used compared with routine stenting (presented at the American College of Cardiology, 2004). However, further study is required to fully evaluate the merits of several techniques that are adjunctive to primary PCI. These include thrombectomy, aspiration, and other emboli protection devices.

The Facilitated Intervention With Enhanced Reperfusion Speed to Stop Events (FINESSE) and ASSENT-4 trials will further elucidate the role of facilitated PCI, the combination of abciximab and a reduced-dose fibrinolytic agent, and the optimal antithrombin agent (enoxaparin vs unfractionated heparin).

Another important area of investigation will be reperfusion injury abatement.

Promising results have been achieved with the use of a complement inhibitor, pexelizumab, during primary PCI. In 960 patients treated with primary PCI, bolus and infusion of pexelizumab resulted in significantly reduced mortality at 90 days (1.8% vs 5.9% with placebo; $P = .014$).[77]

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