Interventional procedures in acute myocardial infarction

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Background Acute myocardial infarction (MI) remains a leading cause of death in the United States. There is evidence that primary (direct) percutaneous intervention (PCI) may improve survival and reduce morbidity in patients with acute MI.

Methods We present a concise, comprehensive, evidence-based literature review of modern techniques of primary PCI in patients with acute MI. A comparison to thrombolytic therapy, especially in selected patient subgroups is made. Rescue angioplasty is also addressed. Adjunctive pharmacology, economic implications, and feasibility of implementation are discussed. A brief discussion of experimental therapies is included.

Results Primary PCI is an acceptable alternative to thrombolytic therapy in patients with acute MI and may result in superior outcomes in select patient populations, especially the elderly, patients with prior coronary artery bypass surgery, those with congestive heart failure, and those in cardiogenic shock.

Conclusions Clinical trials support the use of primary PCI as first-line therapy for acute myocardial infarction. Patients in whom thrombolytic therapy is contraindicated or known to have reduced efficacy are also excellent candidates for this therapy. Ongoing advancements in equipment and adjunctive therapies continue to enhance delivery of this treatment as well as improve patient outcome. (Am Heart J 2001;141:15-24.)
thrombolytic therapy. The incidence of recurrent ischemia was less than 10% in the PTCA arms of the PAMI, ZWOLLE, and GUSTO IIb trials and recurrent MI rates are generally <5% with primary PCI. The incorporation of intracoronary stenting and adjunctive pharmacologic therapy may further reduce these complications.

Weaver et al published a meta-analysis of 10 trials of primary PTCA versus thrombolytic therapy. They showed a 34% relative decrease in mortality as well as significant reductions in death plus nonfatal MI, nonfatal recurrent MI, total stroke, and hemorrhagic stroke (Figure 1).

Selected patient populations

Elderly patients

Elderly patients are known to have a significantly increased mortality rate after acute MI. In the GUSTO 1 trial, the overall mortality rate was 7.0%, but for patients >75 years old the mortality rate was 20.1%. Elderly patients showed a similar increased incidence of stroke and intracranial hemorrhage.

In the PAMI 1 trial a patient aged >65 years was an independent risk factor for the combined end point of death and nonfatal recurrent MI if treated with tissue plasminogen activator (tPA) instead of primary PTCA. In a pooled analysis of the PAMI 1, ZWOLLE, and Mayo Clinic trials, a marked reduction in mortality was noted in elderly patients treated with primary PTCA instead of thrombolytic therapy. Similar reductions in death were seen in patients >70 years old in the GUSTO IIb trial.

Six-month follow-up of 10 randomized trials of primary PTCA versus thrombolytic therapy revealed that patients >60 years old (and diabetics) had the greatest relative reduction in death or nonfatal reinfarction when treated with primary PTCA instead of thrombolytic therapy. Another recent publication suggests that thrombolytic therapy is of limited benefit in patients >75 years old with an acute MI.

Despite these findings, elderly patients undergoing primary PCI still have a higher mortality rate than their younger counterparts do. A recent pooled analysis of the PAMI 2, Stent PAMI and PAMI No Surgery on Site (No SOS) trials showed that patients >75 years old had an in-hospital mortality rate five times higher than those <75 years old.

Cardiogenic shock

Cardiogenic shock has a very poor prognosis if coronary perfusion cannot be quickly restored. Mortality exceeds 80% without treatment. In the Society for Cardiac Angiography Intracoronary Streptokinase Registry, 44 patients with cardiogenic shock were identified. Overall mortality was 66% but reperfusion occurred in only 19 (44%) of these patients. Of the 25 patients with occluded infarct-related arteries, mortality was 84%. In the Gruppo Italiano per lo Studio della Streptochinasi nell’Infarto Miocardico (GISSI 1) and the International Study Group (ISG) trials, the mortality rate for patients with cardiogenic shock was equal to placebo in patients treated with either tPA or streptokinase.

In a review of 14 series of patients with cardiogenic shock, primary PTCA resulted in reperfusion in 60% to
Congestive heart failure

There are data to suggest that the efficacy of thrombolytic therapy is reduced in patients with congestive heart failure (CHF). This may be due to decreased cardiac output resulting in reduced levels of thrombolytic agents reaching the site of intracoronary thrombus, especially when the drugs are given intravenously. In GISSI 1 in-hospital mortality was reduced in class II patients but not in class III patients. At the 6-month follow-up there was no survival benefit over placebo in either group. In the ISG trial no survival benefit was seen in either group.

A recent pooled analysis of the PAMI 2, Stent PAMI, and PAMI No SOS databases revealed that in-hospital and 6-month mortality rates were 7% and 16% for class II patients and 11% and 26% for class III patients, rates considerably lower than in historic controls.

Patients with prior CABG

The mechanism of acute MI in patients with prior CABG is frequently thrombotic occlusion of a saphenous vein graft (SVG). Because the thrombus is often large, it is not surprising that thrombolytic therapy is less effective in these patients. In one small series intravenous thrombolytic therapy restored graft patency in only 25% of cases. With use of primary PCI, O’Keefe et al reported successful recanalization in 86% of infarct-related SVGs. In-hospital mortality was the same in patients with and without prior CABG.

“Rescue” PCI

Rescue PCI refers to procedures performed after failure of full-dose thrombolytic therapy. Multiple trials have shown that success is lower and complications are higher in this setting. The Cohort of Rescue Angioplasty in Myocardial Infarction (CORAMI) investigators attempted rescue PTCA on 72 patients who failed initial thrombolysis. Procedural success was 90% and survival to hospital discharge was 96%.

The recently published Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) trial randomized 302 patients to emergency revascularization (PCI in 64% or coronary artery bypass grafting [CABG] in 36%) or “initial stabilization,” which included the use of intra-aortic balloon counterpulsation or thrombolytic therapy. Overall, all-cause mortality was the same in both groups at 30 days but significantly lower in the revascularization group at 6 months. Patients <75 years old benefitted from early revascularization at both time end points. PCI of the infarct-related occlusion was successful in 78%, and those patients had a 38% mortality rate at 30 days compared with 79% in whom the procedure was unsuccessful.

In the ISG trial no survival benefit was seen in either group. In the TIMI 4 study, 95 (24%) patients had an occluded infarct-related vessel at 90-minute angiography. Fifty-eight patients underwent rescue PTCA (90% successful). Successful rescue PTCA resulted in superior coronary flow and an adverse outcome rate of 29% compared with 83% if rescue PTCA was unsuccessful ($P = .01$).

Ross et al studied 464 patients with failed thrombolysis enrolled in the GUSTO 1 trial compared with 1058 with successful thrombolytic therapy. One hundred ninety-eight patients underwent rescue PTCA. Patients offered PTCA were more likely to be diabetic and had lower left ventricular ejection fractions (LVEF) than did those managed conservatively. LVEF and 30-day mortality were similar among patients with successful rescue PTCA and those managed conservatively.

Finally, Miller et al studied the effectiveness of PTCA with or without abciximab for failed thrombolysis in 392 patients enrolled in the GUSTO III trial. There was no difference in the composite end point of death, stroke, or reinfarction (at 30 days) although there were trends for lower 30-day mortality and increased severe bleeding in patients treated with abciximab. On the basis of these data we generally offer catheter-based reperfusion therapy to patients with failed thrombolytic therapy, especially if any evidence of hemodynamic compromise or electrical instability is present, with the goal of symptom relief and obtaining clinical stability.

Device therapy in acute MI

Intracoronary stents

Initially it was felt that stenting should be avoided in acute MI because of the presence of intracoronary thrombus and the associated systemic hypercoagulable state. With better antiplatelet therapy and reports of successful bailout stenting during PCI for acute MI available, randomized trials of stenting for acute MI were undertaken.

The GR II Stent (Cook, Inc) in Acute MI (GRAMI) trial randomized 65 patients (preliminary results) to primary
PTCA with (40 patients) or without (25 patients) planned stenting. There were no technical failures, reocclusions, or deaths in the stent group. The combined end point of technical failure or death (in-hospital) was significantly lower in the stent group. At the 12-month follow-up, event-free survival was significantly higher in the stent group.

The Florence Randomized Elective Stenting in Acute Coronary Occlusions (FRESCO) trial randomized 150 patients with acute MI and successful PTCA to subsequent stenting versus no further intervention. At 6 months the composite end point of death, reinfarction, or reintervention was 9% in the stent group and 28% in the PTCA group ($P = .003$).

The Stent PAMI trial randomized 900 patients with an infarct-related native coronary artery suitable for stenting to PTCA only or to PTCA followed by intracoronary stenting. At 6 months the composite end point of death, nonfatal MI, disabling stroke, or tricuspid valve replacement (TVR) was lower for the stent group, entirely the result of a lower incidence of ischemia-driven TVR in the stent group. At the 12-month follow-up the composite end point remained significantly lower in the stent group. There was a disturbing trend toward increased mortality in the stent group (5.8% vs 3.7%, $P = .07$), which may be due to the slightly lower initial TIMI 3 flow rate seen after stenting and thought to be due to microembolization of thrombus protruding between the stent struts. Whether this phenomenon will persist with the use of glycoprotein IIb/IIIa receptors is unknown.

Although no mortality benefit has been shown, there is a very significant reduction in the need for repeat target vessel intervention with stenting. Given the large number of procedures performed, this may result in great economic savings.

**Atherectomy devices**

**Rotational atherectomy.** In general, rotational atherectomy (Rotablator, Scimed, Boston Scientific, Boston, Mass) is not recommended in patients with acute coronary syndromes because of the presence of an intracoronary thrombus at the lesion site, which has been shown to result in a high incidence of distal embolization or the no-reflow phenomenon. However, there are several scenarios where rotational atherectomy may be considered. The first is when the culprit lesion cannot be dilated with use of conventional techniques. Often rotational atherectomy (even with a small burr) can modify the lesion and facilitate PCI. Rotational atherectomy can debulk proximal disease to allow reaching the target lesion. Also, one may elect to intervene on a native coronary artery lesion that may be heavily calcified and may benefit from rotational atherectomy.

**Directional atherectomy.** Directional coronary atherectomy (DCA) (Devices for Vascular Intervention, Redwood City, Calif) is a method of selectively removing intraluminal debris from within a coronary artery or graft. There are limited data on the use of DCA as a method of primary percutaneous revascularization in the setting of acute MI. Saito et al compared the results of primary DCA in 21 patients with the results of PTCA in 43 patients with acute MI in which the culprit lesion was in the proximal portion of a nontortuous native coronary artery. Primary DCA was immediately successful in 86% of patients and resulted initially in a larger minimum luminal diameter than did primary PTCA. However, a high rate of restenosis and reocclusion at the 3-month angiographic follow-up negated the beneficial effects of primary DCA.

**Extraction atherectomy.** Transluminal extraction atherectomy (TEC, Interventional Technologies, San Diego, Calif) is a method in which thrombus is aspirated from within the vessel into an extracorporeal collection chamber, thus possibly reducing the risk for distal embolization and no reflow. The TOPIT (TEC vs PTCA in Thrombus) trial randomized patients with acute MI to one of the above therapies. Preliminary results from 250 patients reveal equal efficacy with a lower incidence of major adverse cardiac events (MACE) and fewer non-Q-wave MIs in the TEC group.

**Rheolytic thrombectomy**

The Possis AngioJet (Possis Medical Systems, Inc) consists of a catheter that emits saline jets backward from the tip into an aspiration chamber. The resulting vortex draws thrombus into the catheter. Nakagawa et al published their experience in 31 patients with acute or recent MI. Procedural success was 94% with adjunctive PTCA in 97% and stenting in 40%. Follow-up angiography at 3 to 6 months revealed TIMI 3 flow in all patients and angiographic restenosis in 21% of patients with PTCA and 8% of stented patients.

DeLago et al used the Anjiojet to treat 46 patients with acute MI. Forty-five percent of patients underwent the procedure for failed thrombolysis. Adjunctive stenting was performed in 89% and IIb/IIIa receptor blockers were used in 87% of patients. There were 2 deaths and no strokes or emergency bypass operations during the hospital stay.

**Laser angioplasty**

There is very limited published experience with laser angioplasty in acute MI. Topaz et al reported the results of a multicenter registry of 2038 lesions in 1862 patients treated with a solid-state mid-infrared holmium:YAG laser. Six percent of these patients had acute MI. Laser plus adjunct PTCA achieved a 93% clinical success rate. However, at 6 months no benefit on reducing restenosis was observed.
Ultrasonography

Therapeutic ultrasonography delivered at the site of a thrombus-containing lesion has been proposed as a method of selectively lysing thrombus with minimal disruption of the adjacent arterial wall. Rosenschein and Roth performed ultrasonography in 15 consecutive patients with an acute anterior MI. Ultrasonography alone produced TIMI 3 flow in 87% of the patients. When it was coupled with adjunct therapy, 14 patients had TIMI 3 flow and 1 patient had TIMI 2 flow.

Hamm et al treated 14 patients with acute MI by use of pulsed intracoronary ultrasonography. TIMI flow grade improved at least one grade in 13 of 14 patients and was TIMI grade 3 after adjunctive PTCA (mean 6 ± 2 atm) in all 13 of these patients.

Adjunctive pharmacologic agents

Aspirin

All patients undergoing PCI should receive aspirin (160 mg or greater) unless there is a strong contraindication. Aspirin has been shown to decrease the risk of abrupt closure after PTCA by as much as 50%. For patients who truly cannot take aspirin and are not candidates for desensitization, clopidogrel, 75 mg daily, may be substituted.

Heparin/thrombin inhibitors

Most patients undergoing primary PCI also receive unfractionated heparin (UFH) although there is evidence to suggest that the direct thrombin inhibitor hirudin is an acceptable alternative (especially in patients with a history of heparin-induced thrombocytopenia). Undergoing percutaneous intervention. Furthermore, there is research into using low-molecular-weight heparin, which gives a more predictable level of anticoagulation and obviates the need to monitor activated clotting times.

Ticlopidine/clopidogrel

Patients who receive intracoronary stents require further antiplatelet therapy. In 1996 Hall et al published a study of 220 patients undergoing intravascular ultrasonography (IVUS)–guided stent implantation. One hundred three patients received aspirin alone and 123 received aspirin plus ticlopidine. At the 1-month follow-up, the rate of stent thrombosis was 2.9% and 0.8%, respectively. Schomig et al published a study of 123 patients with acute MI enrolled in the Intracoronary Stenting Antithrombotic Regimen (ISAR) study, which showed a significant reduction in clinical and stent occlusion at 30 days. Bleeding complications were also markedly reduced in the antiplatelet group.

The Full Anticoagulation versus Aspirin and Ticlopidine (FANTASTIC) study and the the Multicenter Aspirin and Ticlopidine Trial after Intracoronary Stenting (MATTIS) trial also showed less stent thrombosis and significant reductions in bleeding and vascular complications with aspirin plus ticlopidine. Recently, Berger has written an excellent review of these studies (Figure 2).

More recently, another thienopyridine derivative, clopidogrel, has been used in place of ticlopidine. The advantages of this compound include more rapid plasma levels after oral loading and substantially fewer side effects, most notably diarrhea, skin rash, and neutropenia. Data are emerging to show that this substitution is safe, although rare cases of thrombotic thrombocytopenic purpura (TTP) have been reported. The Clopidogrel Aspirin Stent Interventional Cooperative Study (CLASSICS) revealed no difference in the composite end point of death, MI, or target lesion revascularization among 740 patients randomized to clopidogrel versus ticlopidine for 28 days (all patients received aspirin).

Glycoprotein IIb/IIIa antagonists

The platelet glycoprotein IIb/IIIa receptor represents the final common pathway in the formation of thrombus. This integrin is responsible for binding to fibrinogen, thereby promoting platelet aggregation.

The first available agent in this class was abciximab, a murine antibody that irreversibly binds to the glycoprotein IIb/IIIa receptor (among others). Later, competitive inhibitors of this ligand were developed (integrilin, tirofiban). There are limited published data with these agents in the setting of primary PCI for acute ST elevation MI.

Lefkovits et al published an analysis of a subgroup of patients in the Evaluation of c7E3 for the Prevention of Ischemic Complications (EPIC) trial. Of the 2099 patients enrolled, 42 underwent primary PTCA for acute MI and 22 for failed thrombolysis. The composite primary end point of death, reinfarction, and repeat intervention or CABG at 6 months was reduced in those randomized to abciximab bolus plus 12-hour infusion compared with placebo. The greatest reduction was in the need for repeat PTCA.

The Reopro and Primary PTCA Organization and Randomized Trial (RAPPORT) randomized 483 patients with acute MI to placebo versus abciximab bolus plus infusion. Abciximab significantly reduced the incidence of death, reinfarction or urgent TVR at 7, 30, and 180 days. There was no benefit on restenosis. In addition, “bailout stenting” was reduced by 42% in the abciximab group.

The Abciximab Before Direct Angioplasty and Stenting in Myocardial Infarction Regarding Acute and Long Term Follow-up (ADIMRAL) trial randomized 300 patients with acute MI undergoing PTCA with or without stenting to placebo versus abciximab bolus plus infusion.
infusion. Preliminary results reveal a 47% reduction in the combined end point of death, recurrent MI, or need for urgent revascularization.

The Controlled Abciximab and Device Evaluation to Lower Late Angioplasty Complications (CADILLAC) trial is a randomized trial involving 2081 patients studying PTCA versus stenting with and without abciximab in patients with acute MI. Preliminary results have shown a lower in-hospital incidence of recurrent ischemia and ischemia-driven TVR in both the PTCA and stent groups when abciximab was used.

Additional benefits of primary PCI

Up-front cardiac catheterization affords the opportunity to assess noninfarct vessels. Both systolic and diastolic function can be rapidly evaluated, as can left-sided valvular structures and the intraventricular septum. Right-heart catheterization adds information concerning right-sided filling pressures, oximetry data, and determination of cardiac output.

These hemodynamic and angiographic data, when combined with clinical assessment, can be extremely useful for post-MI risk stratification. Low-risk patients (those aged <70 years with nonanterior MI, preserved LVEF, favorable coronary anatomy, and stable hemodynamics) can often avoid admission to a coronary care unit and can be discharged expeditiously. High-risk patients, especially those who will require coronary artery bypass surgery, can be identified and referred before hemodynamic compromise or further ischemic complications occur.

Economic considerations

Studies of the cost-effectiveness of primary PCI have shown that this approach is no more costly than a strategy using thrombolytic therapy. Gibbons et al performed a cost analysis of their study, which revealed a trend toward lower hospital costs in the angioplasty group. Six-month follow-up costs were lower with PTCA. Length of hospital stay and readmission rates were also lower in the PTCA group. A detailed analysis of the PAMI I trial revealed that the charges were similar in both groups. The ZWOLLE and GUSTO IIb trials also showed similar costs between the two treatment strategies.

In PAMI 2, low-risk patients (see above) could avoid admission to a coronary care unit and noninvasive testing and could be discharged on the third hospital day. This strategy resulted in a very significant cost savings.

Limitations of primary PCI

Patients with significant renal insufficiency or proteinuria may have a decrement in renal function after the administration of contrast material. There is strong evidence that adequate hydration, conservation of con-
trast, and the use of low osmolar contrast can eliminate much of this risk.60,61

The widespread use of metformin for the treatment of type 2 diabetes mellitus has led to concern about the development of lactic acidosis in patients with compromised renal function who receive intravascular contrast. However, most patients with acute MI can proceed safely to emergency PCI with the immediate discontinuation of metformin and close monitoring of renal function to ensure a return to baseline before the drug is restarted.62

A non-life-threatening contrast reaction requiring therapy occurs in 0.2% to 0.4% of patients. Anaphylactoid reactions occur in 0.04% of patients. Treatment with corticosteroids and antihistamines and changing to a low osmolar contrast medium can lower the incidence of repeat reactions to 0.5%.63 No more than 2 or 3 doses of steroids are generally given to avoid interference with myocardial healing.

Other procedural complications including death, stroke, bleeding, arterial injury (pseudoaneurysm, dissection, perforation), acute closure, stent thrombosis, and distal embolization/no-reflow can occur.

Perceived nonmedical limitations of primary PCI include availability of facilities and competent operators. Trials to assess the safety and efficacy of emergency transport of patients with acute MI to a PCI center have been performed. The Air-PAMI trial compared outcomes in lytic-eligible high-risk patients randomized either to transfer to a tertiary care center for primary PTCA or to local thrombolysis with no routine transfer.64 Despite a delay in time to treatment because of transfer and transportation, there was a 44% decrease in the composite end point of death, recurrent MI, and disabling stroke in the PTCA group. This was not statistically significant as a result of the small sample size. Although encouraging, this strategy cannot be recommended for routine management of acute MI.

There are data regarding the safety of performing PTCA in centers without an on-site cardiac surgery back up.65 The PAMI No SOS trial documented the outcome of 492 high-risk acute MI patients seen at 19 community hospitals performing primary PTCA without cardiac surgery available. A successful result was achieved in 97% of patients undergoing PCI. In-hospital mortality was 2.8% and disabling stroke occurred in 0.4%. At 6 months the composite end point of death, recurrent MI, or disabling stroke was 7.7%, similar to results obtained in experienced interventional laboratories with cardiovascular surgery on site.

The 1999 American College of Cardiology/American Heart Association Guidelines on the Management of Acute Myocardial Infarction66 recommend that (1) balloon dilation occur within 90 ± 30 minutes of the diagnosis of acute MI (increased from ≤90 minutes in the 1996 guidelines67), (2) TIMI grade 2 or 3 flow be established in >90% of patients, (3) emergency CABG rates be <5%, (4) PTCA be performed in >85% of patients with acute MI brought to the catheterization laboratory, and (5) mortality be <12%. With the exception of time delays, these goals were easily achieved in most primary PCI trials. Miller et al showed that these goals could also be obtained in the community hospital setting68 although not all hospitals consistently reach this goal.69

There is evidence that vessel patency rates and clinical outcome are not compromised by a time delay of up to 60 to 120 minutes.70 Berger et al71 showed that in the GUSTO IIb trial time from enrollment to first balloon inflation was an independent predictor of death and that mortality began increasing after 60 minutes. Studies by Cannon et al72 and Liem et al73 suggest that mortality increases and myocardial salvage decreases after a delay of 120 minutes.

It has been suggested that primary PCI should not be performed by low volume operators (<75 cases per year). However, an analysis of the PAMI 2 database revealed no significant differences in the rates of in-hospital death, CABG, or acute PCI success.74 Similar findings were reported in the GUSTO IIb trial.5 A larger study by Ellis et al75 found that, overall, high-volume operators have a lower incidence of major complications but that the difference was not consistent for all operators studied. There is evidence that institutional experience as a whole may influence procedural outcome, with better results achieved in busier centers.71,76

Patient selection and periprocedural care

Once the decision has been made to proceed to angiography and primary PCI, if appropriate, the patient is usually given 325 mg of soluble aspirin along with heparin (American College of Cardiology/American Heart Association guidelines recommend a bolus of 70 U/kg of UFH). Oxygen, nitrates, morphine, and β-blockers are administered as needed for double-product control and pain relief.

If a glycoprotein IIb/IIIa receptor antagonist is to be used, it should be started before the lesion is crossed and the activated clotting time (ACT) titrated to approximately 250 seconds77; otherwise we attempt to keep the ACT between 300 and 350 seconds. In general, we use ionic, low-osmolar contrast medium to minimize hemodynamics. We place an intra-aortic balloon pump only in patients with evidence of sustained hemodynamic compromise or intractable arrhythmias.

Most patients undergo initial PTCA often followed by placement of an intracoronary stent. Usually only the culprit lesion is intervened upon in the acute setting. Other significant stenoses may be treated with a staged procedure once the patient has recovered from the index event.
All patients should be placed on aspirin (usually indefinitely) after PCI unless a definitive contraindication is present. Heparin is generally not continued after the procedure unless balloon counterpulsation is used or the patient is at high risk for an embolic event. Any patient receiving a stent should also be placed on a second antiplatelet agent (clopidogrel or ticlopidine), usually for 4 weeks. Some providers add a second antiplatelet agent for 2 to 4 weeks after PTCa only, but there are no randomized data to support this strategy. β-Blockers, angiotensin-converting enzyme inhibitors, and hypolipidemic agents should be instituted as specified in the American College of Cardiology/American Heart Association Guidelines.86

Low-risk patients (see above) may be transferred to a step-down telemetry unit and usually do not need further risk stratification. Intermediate- and high-risk patients should be initially admitted to a coronary care unit and may require a staged procedure or noninvasive risk stratification before discharge.

Future insights

Many investigators are working on the development of better and easier-to-use stents and other devices. The recently published Plasminogen Activator Coronary Angioplasty (PACT) trial combined half-dose rTPA with planned rescue angioplasty to attempt to achieve a patent artery before PCI.78 In addition, combination drug therapy involving reduced dose thrombolytic therapy and glycoprotein IIb/IIIa receptor antagonists are being studied both as a method of improving pharmacologic reperfusion and as an adjunct to planned PCI (“facilitated angioplasty”).79,80 Strategies to improve myocardial salvage such as inhibition of the sodium-hydrogen exchanger,81 filtration/inhibition of neutrophils,82 and myocardial delivery of hyperbaric oxygen83 are being studied. In addition, the search for methods to reduce restenosis continue.

Conclusion

Primary percutaneous intervention for acute myocardial infarction is both feasible and safe. With the development of easily deployable stents as well as better adjunctive pharmacologic agents, primary PCI can be performed in nearly all patients with acute MI. Continued advances in device and drug therapy will further expand the applicability of this strategy.

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The emerging concept of mitochondrial cardiomyopathies
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Objective  Our purpose was to present an updated review on the spectrum of mitochondrial DNA-related syndromes relevant to cardiac disturbances.

Background  The advent of molecular genetics has provided important insight into the mechanisms underlying a variety of inherited heart disorders, including cardiac arrhythmias and cardiomyopathies. These studies pointed to defects in ion channels, contractile proteins, structural proteins, and signaling molecules as key players in disease pathogenesis, and they have opened up new mechanism-based approaches to therapy.

Results and Conclusions  Mitochondrial DNA defects and faulty oxidative phosphorylation are infrequently considered as causes of cardiomyopathies. This is surprising given the heavy dependence of the heart on oxidative metabolism and the recent advances in understanding the molecular features of mitochondrial disorders. This remarkable progress and the implications it may have for more common forms of cardiovascular disease are reviewed. [Am Heart J 2001;141:e1.]

Direct thrombin inhibitors in acute coronary syndromes and during percutaneous coronary intervention: Design of a meta-analysis based on individual patient data
Direct Thrombin Inhibitor Trialists’ Collaborative Group

Background  More than 30 randomized trials involving more than 40,000 patients with acute coronary syndrome and undergoing percutaneous coronary intervention have evaluated the efficacy and safety of direct thrombin inhibitors relative to unfractionated heparin. However, few trials have been large enough to provide reliable estimates of treatment effects on major cardiovascular outcomes. Therefore uncertainty remains regarding the benefits of direct thrombin inhibitors on major cardiovascular outcomes such as death or myocardial infarction and the balance of any such benefits against the risk of major bleeding.

Objectives  By combining data on individual patients from all the major studies, we sought to obtain reliable estimates of the treatment effects of direct thrombin inhibitors on death, myocardial infarction, major bleeding, and secondary outcomes including refractory or recurrent ischemia and need for revascularization.

We examined these outcomes at the completion of active treatment and during long-term follow-up, as well as in clinically important subgroups.

Methods  Individual patient data, including baseline demographics, previous history of vascular disease, conventional vascular risk factors, qualifying diagnosis, prognostic markers including biochemical markers of extent of myocardial injury, cointerventions, and fatal and nonfatal cardiovascular outcomes, have been obtained from 14 randomized studies, constituting more than 95% of the available randomized evidence. These data will undergo exhaustive data checking for completeness and consistency and will then be merged into a master database for analysis. Analyses will undergo extensive scrutiny by trialists of the direct thrombin inhibitor studies before incorporation into a manuscript. [Am Heart J 2001;141:e2.]