Reperfusion for ST-Segment Elevation Myocardial Infarction
An Overview of Current Treatment Options

Frans Van de Werf, MD, PhD; Donald S. Baim, MD

A 62-year-old man with no prior cardiac history presented to a local community hospital emergency room at 2 AM with 3 hours of chest pain. Initial examination showed a sinus tachycardia at 110 beats per minute, an arterial blood pressure of 100/70 mm Hg, and bibasilar rales. The ECG showed 5 mm of ST-segment elevation across the anterior precordium. Although the hospital had a diagnostic cardiac catheterization laboratory, it did not perform routine coronary angioplasty. A tertiary hospital that offers round-the-clock primary angioplasty was a 30 minute drive by ground ambulance.

The treatment of ST elevation myocardial infarction (STEMI) has undergone important and continuing evolution over the past several decades. Current practice guidelines recognize the importance of promptly restoring normal epicardial blood flow and myocardial perfusion in the infarct zone. In principle, any of several reperfusion strategies might be considered for this patient who was in the early hours of an anterior infarction with evidence of hemodynamic compromise, including pharmacological reperfusion therapy in the community hospital, primary percutaneous coronary intervention (PCI, either in the community hospital or by transport to the tertiary care hospital), or combination therapy, with initiation of reduced-dose pharmacological reperfusion therapy in the community hospital, followed by immediate transport to the tertiary care facility for PCI. Because this patient was at high risk (30 day mortality assumed to be >10% given his extensive anterior infarction and elevated Killip class on admission), the approach that gave the highest chance of achieving early and persistent reperfusion with the lowest risk of major complication should be selected. Each of the proposed therapies offers benefits compared with supportive therapy alone, but the choice among them is complex and still evolving.

Pharmacological Reperfusion Treatment
Prospective randomized trials with various thrombolytic agents have shown a clear mortality reduction compared with supportive therapy (Figure). The currently preferred fibrinolytic regimens are accelerated infusion of alteplase (up to 100 mg/90 minutes), bolus tenecteplase (30 to 50 mg single bolus according to body weight), or reteplase (two 10 U boluses, 30 minutes apart). They should be combined with aspirin 150 to 325 mg orally and unfractionated heparin (60 U/kg bolus [maximum of 4000 U] followed by 12 U·kg⁻¹·h⁻¹ [maximum of 1000 U/h]). If tenecteplase is chosen, the low-molecular-weight heparin enoxaparin (30 mg IV bolus followed by 1 mg/kg subcutaneously every 12 hours, with a maximum of 100 mg for the first 2 subcutaneous injections) may be a better antithrombin agent than unfractionated heparin according to the Assessment of the Safety and Efficacy with a New Thrombolytic Regimen (ASSENT-3) results. In this patient, the risk of intracranial hemorrhage with any of these treatments would be low (<0.75%) given his relatively young age, the absence of a history of hypertension, and a low blood pressure on admission.

An alternative pharmacological reperfusion therapy would be a reduced (half-dose) lytic therapy in conjunction with a platelet glycoprotein IIb/IIIa antagonist, as tested in the large-scale trials Global Utilization of Streptokinase and tPA for Occluded Arteries V (GUSTO-V) (n=16 588) and ASSENT-3 (n=6095), as well as in several smaller angiographic studies. Such combination therapy may increase the speed and quality of reperfusion and reduce the incidence of recurrent ischemia (in-hospital reinfarction, recurrent or refractory ischemia, or urgent PCI), but has not been shown
Evolution of treatment strategies for acute STEMI.

To reduce mortality and may increase spontaneous bleeding complications, especially in the elderly.

**Primary PCI**

Routine immediate angioplasty does not provide an improved outcome after thrombolytic administration, although its selective use to “rescue” patients with persistent or recurrent ischemia after thrombolytic therapy is common. Emergency PCI without thrombolytic therapy (also known as “primary” PCI), however, has been shown to offer a substantial benefit over thrombolytic therapy in terms of the reliability of reperfusion (95% versus 60% restoration of TIMI 3 flow) and event-free survival. A meta-analysis of these trials showed a reduction in 30-day mortality from 6.5% to 4.4%, and a reduction in stroke from 2% to 0.7%, compared with fibrinolytic therapy. Patients with successful primary PCI and no significant hemodynamic or arrhythmic complications of acute myocardial infarction may be admitted to intermediate care units and discharged as early as 3 days post-MI, with a substantial cost saving and preserved favorable outcome. It should be acknowledged, however, that this conclusion reflects performance by highly experienced operators working in centers committed to primary PCI and delivering rapid (<120 minutes) door-to-balloon times. Expansion of primary PCI to community hospitals, with high quality results, is occurring more frequently. Additionally, it should be pointed out that most of these studies used conventional balloon angioplasty (rather than stenting) and excluded higher risk patients who were not candidates for thrombolytic therapy. To extend these findings into the broadest current practice, several issues must thus be addressed.

**Local Hospital Versus Tertiary Center**

When patients present directly to a tertiary center offering PCI, available data suggest that prompt primary angioplasty constitutes optimal therapy for STEMI within 12 hours of symptom onset. Patients presenting to local community hospitals where PCI is not performed appear to benefit from initial transport or rapid transfer to a tertiary center offering primary PCI compared with those receiving thrombolytic therapy given locally, despite the 60 to 90 minute additional treatment delay relating to organization and execution of transfer, on the basis of the results of the AIR-PAMI, Primary Angioplasty in Patients Transferred From General Community Hospitals to Specialized PTCA Units With or Without Emergency Thrombolysis Study (PRAGUE), and DANAMI-2. In the 1572-patient DANAMI-2 trial, 1129 patients presenting to community hospitals were randomly assigned to on-site lytics or transfer to a tertiary hospital for PCI. Those assigned to transfer for PCI showed a comparable benefit in the primary endpoint (death, recurrent infarction, or stroke at 30 days) over those assigned to lytics, as did patients who presented directly to the tertiary hospital (8.5% versus 14.2%, \( P = 0.002 \) for community hospitals; 6.7% versus 12.3%, \( P = 0.048 \) for tertiary hospitals). Because of rapid movement out of the community hospital and concurrent activation of the tertiary hospital PCI team, delay times between presentation and primary PCI were only modestly prolonged (approximately 110 versus 90 minutes) in the transferred patients.

More recently, some community hospitals having cardiac catheterization facilities (but no elective PCI program) have begun to offer primary PCI for acute MI. Using skilled operators who perform elective PCI in nearby tertiary facilities, such hospitals have demonstrated results that comparable to those obtained by primary PCI in tertiary centers and thus preferable to thrombolytic therapy. The decision between local thrombolytic therapy, local primary PCI, and transfer to a primary angioplasty center therefore depends on distance, anticipated time of transfer, patient condition, local community infrastructure, and physician preference, but generally favors primary PCI when feasible.

**Stent or No Stent**

Superior acute angiographic results, procedural safety, and restenosis rates have made elective stent placement the dominant form of PCI, but it is unclear whether the same situation applies for primary intervention. In fact, some early studies raised concerns about an increased incidence of stent thrombosis, slow flow, and 1-year mortality using primary stenting rather than primary conventional balloon angioplasty. More recently, however, studies such as Controlled Abciximab and Device Investigation to Lower Late Angio-
plasty Complications (CADILLAC) have failed to demonstrate any increase in complication rates when stents are used, and in fact have shown a significant benefit in terms of early reoclusion and late restenosis in the infract-related vessel. Current practice thus favors stent implantation during primary intervention.

**Adjunctive Antiplatelet, Antithrombotic, and Thrombolytic Therapy**

Because the precipitating event for acute myocardial infarction is generally thrombus formation on an ulcerated or ruptured plaque, patients undergoing primary angioplasty receive aspirin and heparin as described above. It has been suggested that incremental antiplatelet therapy (ie, glycopro-
tein IIb/IIIa receptor blockers) might attenuate the formation of a new platelet-rich thrombus and thereby improve the outcome of primary intervention. Trial data on this point are still inconclusive, however, with a mortality benefit of intra-
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graft intervention have shown that distal embolization is
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early phases.

The issue of full-dose thrombolytic therapy before imme-
date PCI has been adequately addressed by earlier trials
showing a lack of benefit and (in earlier studies) increased
major complications. Improved revascularization procedures
and sheath management and the use of more fibrin-selective
lytic agents and revised antithrombotic co-therapies have
reduced the risk of complications of PCI performed in the
first hours after the onset of full-dose lytic therapy, but
evidence for improved outcomes after thrombolytic pretreat-
ment before PCI is still inconclusive. Several studies suggest
that pretreatment does result in a greater incidence of infarc
t artery patency on initial angiography, but with trends toward
increased bleeding complications and no conclusive improve-
ment in PCI success or clinical outcome. Additional
adequately-powered trials are now in development to evaluate
this strategy, but pretreatment is most often used selec-
tively when performance of primary PCI is likely to be
delayed by inter-hospital transfer or local logistic
considerations.

Role of Thrombus and Embolus Removal

There is no doubt that an underlying thrombus is present in
the infarct-related artery in patients with STEMI. Such
thrombi can be substantial in size if treatment is delayed or
the vessel is of a large caliber. The AngioJet rheolytic
thrombectomy catheter (Possis Medical, Minneapolis, Minn)
is currently approved for thrombus removal and is com-
monly used in such cases, and other investigational catheters
for thrombus removal or ultrasonic dispersion are being
developed. Trials of these devices for preemptive mechanical
thrombus abatement during acute MI intervention are in their
early phases.

A second issue is persistent abnormal myocardial perfusion
in about 70% of patients in whom normal epicardial flow is
restored. Fragments of thrombus or atherosclerotic plaque
may embolize distally during primary PCI and obstruct the
distal microcirculation, thereby limiting the clinical benefits
of primary PCI. Trials of the Guard Wire embolic protection
device (PercuSurge, Sunnyvale, Calif) during saphenous vein
graft intervention have shown that distal embolization is
ubiquitous and use of the protective device reduces the
incidence of major adverse events and improves postinter-
vension antegrade flow. A similar benefit has been seen in
preliminary registries of acute MI, and a randomized trial is
now in progress to evaluate this indication.

The Role of Myocardial Protection

Although β-receptor blockade is an established therapy to
decrease myocardial oxygen demand and/or reduce arrhyth-
ic complications of STEMI, the main emphasis in treatment
has been on the prompt restoration of myocardial perfusion.
Hemodynamic support (eg, intra-aortic balloon counterpulsa-
tion) may also be beneficial in large infarctions associated
with circulatory compromise, but it has not been shown that
routine balloon pumping enhances myocardial protection
when used in a routine fashion. In contrast, the Should We
Emergently Revascularize Occluded Coronaries for Cardio-
genic Shock (SHOCK) trial does suggest a survival benefit
for patients undergoing coronary intervention, further
strengthening the argument for primary angioplasty in these
high risk patients.

Beyond simple reperfusion, animal data suggest that it may
be possible to limit the amount of myocardial damage further
during the ischemic and the early reperfusion periods. A
variety of pharmacological approaches to prevention of such
injury (including vasodilators, adhesion molecule blockers,
and inhibitors of complement fractions) has been investigated
without showing clear benefit. Recent work with intra-arterial
infusion of super-saturated aqueous oxygen during the reper-
fusion period is of interest, as is the induction of moderate
systemic hypothermia (33°C) via placement of a venous heat
exchange catheter now under evaluation in Cooling as an
Adjunctive Therapy to Percutaneous Intervention in Patients
With Acute Myocardial Infarction (COOL-MI) trial. Thus,
it is likely that the next advances in myocardial recovery will
derive from the combination of prompt definitive mechanical
revascularization (perhaps in association with catheter throm-
bectomy and distal embolic protection), optimal adjunctive
anticoagulant/antiplatelet therapy, and protection of the reper-
fused myocardium by advanced drug/reoxygenation/hypo-
thermic intervention.

Evidence-Based Management
Recommendation

In summary, available evidence suggests that the patient
described above, who presented in the early hours of anterior
infarction with evidence of hemodynamic compromise,
should have undergone reperfusion. Although clear benefit
would have been obtained by thrombolytic administration,
ample data point toward a greater benefit from catheter-based
intervention (primary angioplasty with stent implantation),
either at a qualified community hospital or by transfer to a
nearby tertiary center. Hemodynamic support with intra-
aortic balloon pumping may be required but should not be
performed preemptively. Treatment with platelet glycopro-
tein IIb/IIIa receptor blockers or partial dose thrombolitics
before the primary angioplasty may be used, but definitive
trial data regarding their effectiveness are pending. Still
newer strategies for thrombus removal, distal embolic pro-	ection, and myocardial preservation are enticing, but should
be reserved for participants in well-controlled trials.

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