

Narrative Review: Reperfusion Strategies for ST-Segment Elevation Myocardial Infarction

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Optimal treatment for ST-segment elevation myocardial infarction depends on early diagnosis and rapid selection of the appropriate reperfusion strategy. Primary percutaneous coronary intervention (PCI) is the preferred reperfusion strategy at PCI-capable hospitals. For hospitals without PCI capability, there are 2 reperfusion strategies, primary PCI and thrombolytic therapy, which are both supported by clinical evidence and national guidelines. Transferring patients for primary PCI may cause delays and requires established, proven protocols, systems, and networks to achieve minimal door-to-balloon times. The authors review the available data and present

a systematic, evidence-based approach in a simple framework to enable noncardiovascular and cardiovascular physicians to select the optimal reperfusion strategy. The framework is based on available data from clinical trials and local circumstances from clinical practice by incorporating duration of symptoms (fixed ischemia time) and anticipated transport delays to a PCI-capable facility (incurred ischemia time).

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A 72-year-old woman presents to a community hospital with substernal chest pain that started 2 hours previously. She has no history of cardiac disease, and the results of initial 12-lead electrocardiography show 4-mm ST-segment elevation in leads V2 to V6. Physical examination shows a diaphoretic woman in moderate distress with a heart rate of 98 beats/min and blood pressure of 94/60 mm Hg. Jugular venous pressure is normal, lung fields are clear, and cardiac examination reveals no gallops or murmurs. Her extremities are warm. The closest tertiary hospital with a cardiac catheterization laboratory is 70 miles away. How should the patient be managed?

THE CLINICAL PROBLEM

Coronary artery disease is a leading cause of morbidity and mortality in developed and developing nations. Each year, more than 500 000 Americans have acute myocardial infarction (MI) with ST-segment elevation (STEMI) or new left-bundle-branch block (1). Reperfusion to achieve early, complete, and sustained blood flow leads to optimal outcomes. Delays in restoring blood flow, regardless of the reperfusion method, are associated with adverse outcomes, including death and depressed left ventricular function.

The American Heart Association (AHA)/American College of Cardiology (ACC) guidelines (1) and the European Society of Cardiology guidelines for ST-segment elevation MI (2) collate a large body of data; however, translating guidelines into clinical practice at acute care hospitals with and without percutaneous coronary intervention (PCI) capability remains challenging. For hospitals with on-site PCI capability, reperfusion with primary PCI provides the best outcomes if door-to-balloon times of less than 90 minutes, and preferably less than 60 minutes (3, 4), can be achieved consistently. For hospitals without PCI capability, potential reperfusion strategies include immediate thrombolysis, transfer for primary PCI, and so-called thrombolytic-facilitated PCI. The delays, risks, and benefits associated with each reperfusion strategy must be carefully considered (5–8). Selection of a reperfusion strategy

at hospitals without PCI capability remains controversial, and substantial variations exist in clinical care.

STRATEGIES AND EVIDENCE

The **Figure** and **Table 1** show a systematic framework for selecting reperfusion strategies in STEMI that allows for integration of evidence-based data into local circumstances (relationships between physicians and hospitals with and without on-site surgery, state regulatory requirements, emergency medical services transport capability and availability, and implementation of protocols for myocardial infarction). All patients presenting to the emergency department with chest pain should have electrocardiography immediately and, at most, within 5 to 10 minutes. If ST-segment elevation MI is confirmed, a reperfusion strategy based on resource availability and patient risk should be rapidly implemented.

Patients with ST-segment elevation MI presenting to PCI-capable hospitals should have primary PCI with a target door-to-balloon time of less than 90 minutes. If the hospital does not have PCI capability, the clinician must first determine whether the patient is eligible for thrombolytic therapy (**Table 2**). Patients who are not eligible for such therapy and those in cardiogenic shock should be given oxygen, aspirin, and heparin and should be transferred for primary PCI. For patients who are eligible for thrombolytic therapy, the clinician must consider 2 important factors: duration from onset of symptoms (fixed ischemia time) and anticipated transport time to the nearest PCI-capable facility (incurred ischemia time). These 2 fac-

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tors can be incorporated into a 2 × 3 table to select the optimal reperfusion strategy (Table 1).

If the anticipated transport time is less than 30 minutes, the patient should be transferred for primary PCI, regardless of the duration of symptoms. Patients who are eligible for thrombolytic therapy, who present less than 3 hours from onset of symptoms, and who will have a transport time of more than 30 minutes should receive thrombolytic therapy, and those who present 3 to 12 hours after the onset of chest pain and will have a transport time of less than 60 minutes should be transported for primary PCI. If the anticipated transport time is more than 60 minutes, patients may be treated with thrombolytic therapy or primary PCI. If primary PCI is intended but is not possible because of coronary anatomy, mechanical complications of MI, or technical problems, then hemodynamic support with an intra-aortic balloon pump and urgent coronary bypass surgery should be considered and weighed against the alternative of conservative medical management.

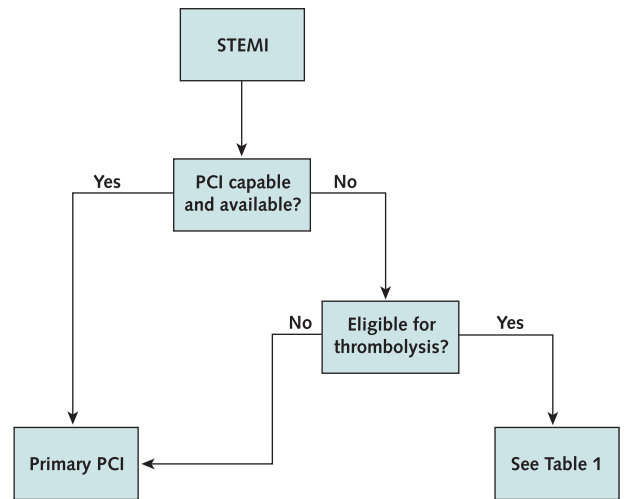
All patients receiving thrombolytic therapy should be transferred to a PCI-capable facility in case of reperfusion failure (ongoing chest pain or <70% resolution of ST-segment elevation at 90 minutes) and the need for so-called rescue PCI, which can be anticipated to occur in 30% to 40% of patients. Data from the multicenter randomized Rescue Angioplasty versus Conservative Treatment or Repeat Thrombolysis (REACT) trial showed that patients who experience failure of thrombolytic therapy and are treated with rescue PCI have better event-free survival than those treated with conservative treatment or repeat thrombolysis (9). In addition, the Routine Invasive Strategy within 24 hours of Thrombolysis versus Ischaemia-Guided Conservative Approach for Acute Myocardial Infarction with ST-Segment Elevation (GRACIA-1) trial suggested that patients with ST-segment elevation MI who are treated with thrombolytic therapy benefit from routine coronary angiography and PCI if indicated within 24 hours of thrombolysis (10).

GUIDELINES AND CLINICAL DATA

Thrombolysis versus Primary PCI in a Hospital with PCI Capability

Thrombolytic therapy for ST-segment elevation MI has been shown to be effective in randomized trials involv-

Figure. Algorithm for selecting a management strategy in patients with ST-segment elevation myocardial infarction (STEMI).



PCI = percutaneous coronary intervention.

ing more than 100 000 patients (11). When thrombolytic therapy is administered with aspirin, approximately 50 lives are saved per 1000 patients treated (12). Although such therapy is widely available, easily administered, and cost-effective, important limitations exist: Only 50% to 60% of patients with ST-segment elevation MI are eligible (Table 2), and only 60% to 70% of those will achieve complete reperfusion. In addition, 10% to 20% of patients will experience reocclusion of the infarct vessel and 1% to 2% will have a stroke or intracranial hemorrhage (13).

Primary PCI achieves complete reperfusion in 90% to 95% of patients; is associated with a lower risk for stroke; and allows definitive characterization of coronary anatomy, left ventricular function, and mechanical complications. Several randomized trials have compared thrombolytic therapy with primary PCI in patients with ST-segment elevation MI (14–36). In a meta-analysis of 23 trials with 7739 randomly assigned patients (37), primary PCI was associated with an incremental 20 lives saved per 1000 patients treated (30-day mortality rate, 7% vs. 9%; *P* =

*Table 1. 2 × 3 Framework for Selecting a Reperfusion Strategy for Patients with ST-Segment Elevation Myocardial Infarction**

Transport Time (Incurred-Ischemia Time)	Duration of Onset of Symptoms (Fixed Ischemia Time)	
	<3 h	>3 h
<30 min	Primary PCI and GP IIb/IIIa†	Primary PCI and GP IIb/IIIa†
30–60 min	Thrombolytic agent and clopidogrel‡	Primary PCI and GP IIb/IIIa†
>60 min	Thrombolytic agent and clopidogrel‡	Thrombolytic agent and clopidogrel or primary PCI and GP IIb/IIIa‡

* Patients treated with thrombolytic agents should be immediately transferred to a PCI-capable facility in the event of failure to reperfuse. GP IIb/IIIa = platelet glycoprotein IIb/IIIa inhibitor; PCI = percutaneous coronary intervention.
 † Based on American Heart Association/American College of Cardiology guidelines.
 ‡ Based on clinical trials.

Table 2. Absolute and Relative Contraindications for Thrombolytic Therapy in Patients with ST-Segment Elevation Myocardial Infarction

Absolute contraindications

Any previous intracranial hemorrhage
 Known structural cerebral vascular lesion
 Known malignant intracranial neoplasm
 Ischemic stroke within the past 3 months (except for acute stroke within 3 hours)
 Suspected aortic dissection
 Active bleeding or bleeding diathesis (excluding menses)
 Significant closed-head or facial trauma within 3 months

Relative contraindications

History of chronic, severe, or poorly controlled hypertension
 Severe uncontrolled hypertension on presentation (systolic blood pressure >180 mm Hg or diastolic blood pressure >110 mm Hg)
 History of ischemic stroke more than 3 months previously, dementia, or known intracranial disorders not covered in absolute contraindications
 Traumatic or prolonged cardiopulmonary resuscitation (>10 minutes) or major surgery (within past 3 weeks)
 Recent internal bleeding (within past 2 to 4 weeks)
 Noncompressible vascular punctures
 Pregnancy
 Active peptic ulcer
 Current use of anticoagulant agents: the higher the international normalized ratio, the higher the risk for bleeding
 Previous exposure (>5 days earlier) to or previous allergic reaction to streptokinase or anistreplase

0.0002); less reinfarction (3% vs. 7%; $P = 0.0001$); and fewer strokes (1% vs. 2%; $P = 0.0004$) at 30 days, compared with thrombolytic therapy. Percutaneous coronary intervention capability, however, is available at fewer than 50% of U.S. hospitals; requires substantial investment in infrastructure, personnel, and training; and requires maintenance of procedural volume and expertise for physicians and allied health staff (38, 39).

On the basis of these data, patients with ST-segment elevation MI who present to hospitals with PCI capability should have primary PCI as soon as possible, with target door-to-balloon times of less than 90 minutes. Keys to consistently achieving these targets include obtaining pre-hospital electrocardiograms; enabling emergency department physicians to activate the catheterization laboratory directly; and developing service-level agreements across the continuum of care encompassing the emergency department, catheterization laboratory, and coronary care unit (3, 4).

Thrombolysis versus Primary PCI in a Hospital without PCI Capability

The management of patients with ST-segment elevation MI who present to hospitals without PCI capability is more controversial because transfer to a PCI-capable facility may be associated with substantial delays before reperfusion. For example, median door-to-balloon times in the National Registry of Myocardial Infarction (NRM) registry for patients transferred for primary PCI was 180 minutes (4), which is well above acceptable limits.

Patients Less than 3 Hours from Symptom Onset

The success rate of thrombolytic therapy is inversely correlated with duration of symptoms. Success is greatest during the first “golden hour,” in which thrombolytic agents have the potential to abort MI (40, 41). In a sub-study of 460 patients from the Comparison of Angioplasty and Prehospital Thrombolysis in Acute Myocardial Infarction (CAPTIM) trial who presented within 2 hours of onset of chest pain, those treated with thrombolytic agents had lower mortality rates than those who had primary PCI (2.2% vs. 5.7%; $P = 0.058$) and a lower incidence of cardiogenic shock (1.3% vs. 5.3%, $P = 0.032$) (42).

The Danish Multicenter Randomized Study on Thrombolytic Therapy versus Acute Coronary Angioplasty in Acute Myocardial Infarction (DANAMI) 2 trial showed that patients treated with primary PCI had a 46% relative risk reduction in the 30-day combined end point of death, reinfarction, or disabling stroke compared with those treated with thrombolytic therapy (33). This benefit was consistent among patients presenting less than 2 hours, 2 to 4 hours, and more than 4 hours from symptom onset (33). Of importance, the median transport time was only 32 minutes—a benchmark difficult to achieve in other geographic areas.

These data suggest that patients with ST-segment elevation MI who present to PCI-incapable hospitals within 2 to 3 hours after symptom onset should be treated with thrombolytic agents if transfer time is greater than 30 minutes but should be transferred for primary PCI if the anticipated transfer time is reliably less than 30 minutes. All patients with contraindications to thrombolytic therapy or those in cardiogenic shock should be transferred for primary PCI. The current AHA/ACC guidelines for ST-segment elevation MI recommend thrombolytic therapy for patients who present less than 3 hours from symptom onset and have delay to PCI, defined as door-to-balloon time minus door-to-needle time greater than 60 minutes or door-to-balloon time greater than 90 minutes (1).

Patients More than 3 Hours from Symptom Onset

The AHA/ACC guidelines for ST-segment elevation MI recommend that patients presenting more than 3 hours from symptom onset or high-risk patients with cardiogenic shock, Killip class 3 or greater, age older than 75 years, or anterior infarct be transferred for primary PCI (1). For patients with symptom duration greater than 3 hours and a transfer time less than 60 minutes, primary PCI is the preferred treatment (22, 30, 33, 36).

Management options are less clear for patients with an anticipated transport time greater than 60 minutes. Although thrombolytic therapy is less effective more than 3 hours from symptom onset, a demonstrable mortality benefit exists up to 12 hours (41). Three trials comparing thrombolytic therapy versus transfer for PCI in patients presenting up to 12 hours from the onset of chest pain are

Table 3. Trials Comparing In-Hospital Thrombolysis versus Transfer for Percutaneous Coronary Intervention in Patients Presenting Less than 12 Hours from the Onset of Chest Pain*

Study, Year (Reference)	Patients, n	Death, Reinfarction, or Disabling Stroke at 30 Days, %		P Value
		Thrombolysis	Transfer for PCI	
Widimský et al., 2003 (22)	850	15.2	8.4	<0.003
Grines et al., 2002 (36)	138	13.6	8.4	0.33
Andersen et al., 2003 (33)	1572	13.7	8.0	<0.001

* PCI = percutaneous coronary intervention.

summarized in Table 3. The combined end point of death, reinfarction, and disabling stroke at 30 days was lower in patients treated with primary PCI. Recent data suggest that patients presenting more than 12 hours from symptom onset may also benefit from primary PCI (43).

The major disadvantage of transferring patients for primary PCI is delaying reperfusion, or incurred ischemia time. Each 30-minute delay from symptom onset to balloon inflation is associated with a 7.5% increase in death at 1 year (44), and any mortality benefit of primary PCI may be lost if the door-to-balloon time is 60 minutes more than the door-to-needle time for thrombolytic therapy (45). Therefore, patients who present 3 to 12 hours from symptom onset with an anticipated transport time greater than 60 minutes can be managed with thrombolysis or can be transferred for primary PCI depending on their risk profile and comorbid conditions, anticipated transport delay, and availability of local resources. Neither reperfusion strategy has been conclusively shown to be superior in this setting.

Glycoprotein IIb/IIIa Inhibitors

Glycoprotein IIb/IIIa inhibitors are potent parenteral agents that inhibit the final common pathway for platelet aggregation. Currently 3 agents are available: abciximab, eptifibatide, and tirofiban.

Use with Thrombolytic Therapy

Thrombolysis is a potent activator of platelets (46), and concomitant use of aspirin is mandatory. (12). On the basis of promising pilot studies (47, 48), 3 randomized trials (Table 4) investigated combination therapy with a glycoprotein IIb/IIIa inhibitor and half-dose thrombolytic therapy for ST-segment elevation MI (49–51). The largest

of these trials, the 16 588-patient Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO) V trial, found no mortality benefit over a standard thrombolytic regimen at 30 days (mortality rate, 5.6 % for abciximab and half-dose reteplase vs. 5.9% for full-dose reteplase; *P* = 0.43) (49). Patients treated with combination therapy had higher rates of major bleeding (1.1% vs. 0.5%; *P* < 0.0001) and minor bleeding (20% vs. 11.4%; *P* < 0.0001) (49). This increased bleeding risk and lack of mortality benefit with combination therapy was also found in 2 other trials (50, 51) (Table 4). On the basis of these results, glycoprotein IIb/IIIa inhibitors should not be used in combination with thrombolytic therapy, aspirin, and heparin.

Use with Primary PCI

Among patients having elective and urgent PCI (52), use of glycoprotein IIb/IIIa inhibitors is associated with a 31% relative risk reduction (0.90% vs. 1.37%) for death at 30 days. In a meta-analysis of 8 trials, adjunctive therapy with abciximab during primary PCI was associated with lower mortality rates (2.4% vs. 3.4%; *P* = 0.047) and reinfarction rates (1.0% vs. 1.9%; *P* = 0.030) compared with placebo at 30 days (53).

In patients presenting with ST-segment elevation MI, the administration of glycoprotein IIb/IIIa inhibitors before arrival at the catheterization laboratory (Table 5) is associated with a higher prevalence of Thrombosis in Myocardial Infarction (TIMI) 2 or 3 flow (41.7% vs. 29.8%; *P* < 0.001) of the infarct-related artery (62). On the basis of these data and the known association of TIMI 2 or 3 flow before PCI with fewer in-hospital events and better

Table 4. Randomized Trials Comparing Combination Therapy with a Glycoprotein IIb/IIIa Inhibitor plus Half-Dose Thrombolytic Therapy and Full-Dose Thrombolytic Agents in Patients with ST-Segment Elevation Myocardial Infarction

Study, Year (Reference)	Patients, n	Glycoprotein IIb/IIIa Inhibitor	Thrombolytic Agent	Mortality Rate, %		Major Bleeding Rate, %	
				Combination Therapy	Thrombolytic-Only Therapy	Combination Therapy	Thrombolytic-Only Therapy
Topol, 2001 (49)	16 588	Abciximab	Reteplase	5.6	5.9	1.1	0.5*
Van der Werf et al., 2001 (50)	6095	Abciximab	Tenecteplase	6.6	6.0	4.3	2.2*
Ciugliano et al., 2003 (51)	438	Eptifibatide	Tenecteplase	3.0	5.0	7.6	2.5

* *P* < 0.001.

Table 5. Studies Comparing Early versus Late Administration of Glycoprotein IIb/IIIa Inhibitors in Patients with ST-Segment Elevation Myocardial Infarction Having Primary Percutaneous Coronary Intervention*

Study, Year (Reference)	Patients, <i>n</i>	Agent	Patients with TIMI 2 or 3 Flow, %		P Value
			Early Administration	Late Administration	
Zorman et al., 2002 (54)	112	Abciximab	32	13	0.040
Arntz et al., 2003 (55)	100	Abciximab	52	48	NS
Mesquita Gabriel et al., 2003 (56)	74	Abciximab	31	26	NS
van't Hof et al., 2004 (57)	307	Tirofiban	43	34	0.040
Lee et al., 2003 (58)	100	Tirofiban	46	18	0.007
Cultrip et al., 2003 (59)	58	Tirofiban	39	27	NS
Cultrip et al., 2001 (60)	60	Eptifibatide	57	13	<0.001
Zeymer et al., 2005 (61)	102	Eptifibatide	42	33	0.010

* NS = not significant; TIMI = Thrombolysis in Myocardial Infarction.

1-year outcomes (62–65), glycoprotein IIb/IIIa inhibitors should be administered before the patient arrives at the catheterization laboratory. The early use of glycoprotein IIb/IIIa inhibitors is supported by the AHA/ACC guidelines for ST-segment elevation MI (1). Although these guidelines support the use of any of the 3 agents, abciximab is favored because of the substantially greater amount of data on this agent in the setting of PCI for ST-segment elevation MI. Abciximab, however, may not be available at hospitals without PCI facilities because it is only indicated for PCI, whereas the other 2 agents are also indicated for unstable angina and non-ST-segment elevation acute coronary syndromes (66).

Clopidogrel

Clopidogrel is an oral thienopyridine prodrug whose active metabolite inhibits platelet activation by interaction with the P2Y12 adenosine diphosphate receptor.

Use with Thrombolytic Therapy

In the Clopidogrel as Adjunctive Reperfusion Therapy (CLARITY)-TIMI 28 trial (67, 68), 3491 patients with ST-segment elevation MI who were 75 years of age or younger and treated with thrombolytic agents and aspirin were randomly assigned to placebo versus clopidogrel (300-mg loading dose and 75 mg/d thereafter). The composite primary end point of death, reinfarction, or occlusion of the infarct-related artery at angiography occurred in 15% of patients randomly assigned to clopidogrel and 22% of those in the placebo group (*P* < 0.001) (60). Clopidogrel was not associated with a higher rate of bleeding.

The Clopidogrel and Metoprolol in Myocardial Infarction (COMMIT) trial (69) randomly assigned 45 849 patients with MI (39 755 with ST-segment elevation MI) to aspirin versus aspirin and clopidogrel (75 mg/d without a loading dose). This trial included patients who were 75 years of age or older, and there was no exclusion criteria based on age. Patients treated with clopidogrel had a lower rate of the composite end point of death, reinfarction, or stroke (9.3% vs. 10.1%; *P* = 0.002) and no increase in bleeding. These data suggest that patients with ST-segment

elevation MI who are treated with thrombolytic agents, aspirin, and heparin should also receive clopidogrel, 75 mg/d, with a loading dose of 300 mg for those 75 years of age or younger.

Use with Primary PCI

Although clopidogrel is used routinely as adjunctive therapy for intracoronary stenting, currently no data from randomized, controlled trials are available to address the early administration of clopidogrel before coronary angiography in patients with ST-segment elevation MI having primary PCI. Therefore, clopidogrel should not be used in patients with STEMI having primary PCI before visualization of the coronary anatomy.

COMORBID CONDITIONS AND SELECTION OF REPERFUSION

The AHA/ACC guidelines for ST-segment elevation MI highlight patient risk and comorbid conditions that may influence selection of a reperfusion strategy (1). If primary PCI can be performed without substantial delay, then this reperfusion strategy is generally preferred in patients who are elderly (≥75 years of age), in cardiogenic shock, with Killip class 3 or greater, with pulmonary edema, with anterior wall infarction, or at increased risk for bleeding. Although primary PCI is preferred in patients 75 years of age or older, being elderly is not in itself an absolute or relative contraindication to thrombolytic therapy. An invasive strategy is also preferred if the diagnosis of ST-segment elevation MI is in doubt and other diagnoses, such as pericarditis, myocarditis, aneurysm, or apical ballooning, are being considered. Patients with peripheral arterial disease in whom vascular access is extremely difficult may be better treated with thrombolysis.

AREAS OF UNCERTAINTY

Three trials have investigated pretreatment with full-dose or half-dose thrombolytic therapy in patients who may experience delays before PCI. In the Bavarian Reper-

fusion Alternatives Evaluation (BRAVE) study, 253 patients with ST-segment elevation MI having primary PCI were randomly assigned to pretreatment with abciximab versus abciximab and half-dose reteplase (70). Infarct size was similar (11.5% in the abciximab group vs. 13% in the combination group; $P = 0.81$), and no difference was observed in the incidence of death, recurrent MI, or stroke (4.7% in the abciximab group vs. 6.4% in the combination group; $P = 0.56$). Major bleeding complications were more frequent in the combination group, although this was not statistically significant (1.6% in the abciximab group vs. 5.6% in the combination group; $P = 0.16$).

Among patients with ST-segment elevation MI, the potential for harm cannot be overlooked. The Assessment of the Safety and Efficacy of a New Treatment Strategy with Percutaneous Coronary Intervention (ASSENT) 4 trial was halted after 1667 of the 4000 planned patients were enrolled (71). Interim analysis showed that pretreatment with full-dose tenecteplase followed by PCI led to increased in-hospital deaths compared with primary PCI alone (6% vs. 3%; $P = 0.010$) (71). Patients in the thrombolytic-facilitated PCI group also had a greater incidence of stroke (1.8% vs. 0%; $P < 0.001$) and reinfarction (6% vs. 4%; $P = 0.028$). The median time from symptom onset to randomization was 140 minutes in the tenecteplase-facilitated PCI group and 135 minutes in the PCI-alone group ($P = 0.55$). The median time from symptom onset to balloon time was 263 minutes in the tenecteplase-facilitated PCI group and 255 minutes in the PCI-alone group ($P = 0.72$).

The use of full-dose thrombolytic-facilitated PCI should be avoided, according to data from ASSENT 4. These data are supported by a recent meta-analysis (72). The use of a half-dose thrombolytic-facilitated PCI is currently being investigated in the ongoing Facilitated Intervention with Enhanced Reperfusion Speed to Stop Events (FINESSE) trial and should not be used outside the context of a randomized clinical trial.

CONCLUSIONS AND FUTURE DIRECTIONS

Optimal treatment of patients with ST-segment elevation MI hinges on prompt diagnosis and rapid selection of the appropriate reperfusion strategy. A systematic approach to select the optimal reperfusion strategy according to duration of symptoms (fixed ischemia time) and inherent delays for transport to a PCI-capable facility (incurred ischemia time) is presented. An evidence-based framework (Figure and Table 1) that is easy and practical to implement can be used for the rapid selection of the preferred reperfusion strategy and adjunctive pharmacotherapy. Because of the potential for harm, therapies and reperfusion strategies that have not been rigorously studied should not be used outside the auspices of a clinical research trial with informed consent from the patient. The presented frame-

work can be easily updated as new data and reperfusion strategies become available.

Opportunities for improvements to decrease fixed ischemia time include obtaining prehospital 12-lead electrocardiograms and increasing public education and awareness of the signs and symptoms of a heart attack. Opportunities for improvements to decrease incurred ischemia time include enabling the emergency department physician to activate the catheterization laboratory directly; developing protocols, systems, and networks to expedite patient transfer; implementing faster helicopters for transport; and carefully evaluating the role of primary PCI at hospitals without on-site cardiac surgery.

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