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Timeliness of treatment is more important than choice of reperfusion therapy

Reperfusion therapy decreases morbidity and mortality rates in patients with ST-segment elevation myocardial infarction (MI). Primary percutaneous coronary intervention (PCI) is preferred over fibrinolytic therapy as a reperfusion strategy when the delay in the time to treatment is short and the patient presents to a high-volume, well-equipped center with expert interventional cardiologists.

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Compared with fibrinolytic therapy in randomized clinical trials, primary PCI produces higher rates of infarct artery patency, complete reperfusion (grade 3 by the criteria of the Thrombolysis in Myocardial Infarction [TIMI] study), and access-site bleeding. It also produces lower rates of recurrent ischemia, reinfarction, emergency repeat revascularization procedures, intracranial hemorrhage, and death.[1] If performed early and successfully, primary PCI also greatly decreases the rates of complications of ST-elevation MI that result from longer ischemic times or unsuccessful fibrinolytic therapy, allowing earlier hospital discharge and resumption of daily activities. Primary PCI is also the best reperfusion option in patients who present late after the onset of symptoms and in patients with cardiogenic shock, and it is the only option in patients who have contraindications to fibrinolytic therapy because of bleeding risk.

However, most hospitals do not have PCI capability. Two options at these hospitals are to transfer the patient to a PCI center quickly for primary PCI or to keep the patient on site and give fibrinolytic therapy, with its limitations. Earlier trials suggested that the transfer strategy was superior, but they had limitations: most patients received streptokinase, an inferior fibrinolytic agent, and door-to-door-to-balloon times were rapid, averaging only 95 minutes because of excellent logistical protocols and careful patient selection.[2] Most importantly, rescue PCI and routine PCI were seldom performed in patients receiving fibrinolytics, so fibrinolytic therapy was being tested as monotherapy.

In the real world, however, treatment delays are much longer, and fibrinolytic therapy has evolved into a strategy that includes crossover to rescue PCI or routine PCI. Therefore, the initial trials of transfer for primary PCI do not reflect current practice. In fact, recent registry data suggest that prehospital fibrinolytic therapy followed by early angiography is superior to primary PCI because most patients can be treated within 2 hours of symptom onset; they also suggest that on-site fibrinolytic therapy followed by early angiography is equal in efficacy to primary PCI as long as rescue PCI and routine PCI can be performed.[3,4]

The most important modifiable predictor of outcome is the time to treatment

The most important modifiable predictor of outcome in ST-elevation MI is the time to treatment, a biological truth that continues to be supported by clinical evidence despite ideologic arguments by some interventional

The author has disclosed membership on a clopidogrel advisory board for Sanofi-Aventis and Bristol-Myers Squibb.

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cardiology enthusiasts who claim that primary PCI is always superior to the fibrinolytic strategy, regardless of delays.

SURPRISINGLY, OUTCOMES WERE WORSE WITH FACILITATED PCI

It made sense, then, to conclude that the perfect strategy for hospitals without PCI capability would be a combined strategy of immediate fibrinolytic therapy to decrease the time delay associated with organizing PCI, and rapid transfer for immediate PCI to improve the limited reperfusion rates associated with fibrinolytic therapy.

Surprisingly, though, randomized trials found worse outcomes with this "facilitated PCI" strategy.[5]

Again, limitations in trial design might explain the lack of benefit in the trials. Inadequate anticoagulant and antiplatelet therapy were given to the fibrinolytic patients, and primary PCI patients had relatively short treatment delays, with many patients enrolled at hospitals with PCI capability.

PROGRESS IN REPERFUSION THERAPY

Great strides have been made in reperfusion therapy in recent years. Adjunctive therapy with clopidogrel (Plavix) and enoxaparin (Lovenox) has been shown to improve outcomes with fibrinolytic therapy. Bivalirudin (Angiomax) and stents have improved primary PCI's performance. Reducing bleeding complications has become a clinical priority, with increasing emphasis on adjusting some drug doses according to renal function and using the radial artery for cardiac catheterization.

Today, the goal is to treat every patient with the best reperfusion strategy available

The American College of Cardiology initiative, "Door-to-Balloon (D2B): An Alliance for Quality," focused much attention on organizing in-hospital systems of care for primary PCI, thus increasing the national rate of achieving a door-to-balloon time within 90 minutes from 50% to over 75% in patients who presented to hospitals with PCI capability.[6]

The American Heart Association has launched "Mission: Lifeline," a national campaign to organize prehospital systems of care with their program,[7] working within communities to address their unique needs, resources, and barriers to implementing systems of care for ST-elevation MI. The key aspect of this effort is to help geographic regions develop local solutions, an explicit recognition that there is no one-size-fits-all solution. Early triage by emergency medical services, rapid diagnosis with prehospital electrocardiography, destination and interhospital transfer protocols, and prehospital activation of the cardiac catheterization laboratory can greatly streamline emergency care and decrease treatment delays for primary PCI.

FOR OUTLYING HOSPITALS, A PHARMACOINVASIVE STRATEGY

So what about hospitals without PCI capability that cannot routinely transfer patients to a hospital with PCI capability within 90 minutes?

Lessons learned from the experiences with immediate PCI, rescue PCI, and facilitated PCI have evolved into the "pharmacoinvasive strategy." Patients with ST-elevation MI are treated as rapidly as possible with a bolus of a fibrinolytic drug, eg, tenecteplase (TNKase) or reteplase (Retavase), and are also given aspirin, clopidogrel, and enoxaparin. Then, they are rapidly transferred to a PCI-capable hospital so that emergency PCI can be performed if reperfusion is not clinically apparent or if the patient develops pulmonary edema or cardiogenic shock. If the clinical signs suggest that reperfusion has been achieved (relief of chest pain, rapid resolution of ST-segment elevation, bursts of accelerated idioventricular rhythm), coronary angiography (and PCI, if indicated) can be performed within 3 to 24 hours of fibrinolytic therapy. This time frame allows the initial fibrinolytic effect to dissipate, while the antiplatelet and anticoagulant drugs achieve therapeutic levels.

Today, the goal is to treat every patient with the best reperfusion strategy available, given the limitations in resources and the geographic location of some centers, and to maximize the possibility of sustained patency of the infarct-related artery by implanting a stent, even if it takes several hours and transfer to another hospital to perform PCI.[8] The pharmacoinvasive strategy of rapid administration

of fibrinolytic therapy followed by PCI within 24 hours would be practical in most hospitals without PCI capability where treatment delays prohibit performance of primary PCI within 90 minutes of first medical contact.[9]

THE 'STREAM' TRIAL IS UNDER WAY

As proof of concept, the Strategic Reperfusion Early After Myocardial Infarction (STREAM) trial is enrolling 2,000 patients with ST-elevation MI presenting within 3 hours of symptom onset if primary PCI is not feasible within 60 minutes of first medical contact.[10] Patients will be randomized to either of the following:

- Receive prehospital therapy with tenecteplase, aspirin, clopidogrel, and enoxaparin and undergo cardiac catheterization in 6 to 24 hours (or rescue PCI if reperfusion fails within 90 minutes of fibrinolysis)
- Undergo primary PCI performed according to local guidelines.

The primary measure of efficacy will be the composite rate of death, cardiogenic shock, heart failure, and reinfarction at 30 days. Measures of safety include the rates of ischemic stroke, intracranial hemorrhage, and major nonintracranial bleeding.

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Charcot neuroarthropathy **1C 2A**
Hepatitis C **1C 2C**
Tuberculosis tests **1D 2C**
Myocardial infarction **1B 2D**