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Medi Quest BRS Hospital

A monthly News letter from BRS Hospital

MYOCARDIAL INFARCTION

DIAGNOSIS, COMPLICATIONS & MANAGEMENT - PART (2/3)

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Fibrinolysis for MI

Most cases of Acute Myocardial Infarction are caused by Coronary Artery plaque rupture with subsequent thrombus formation. When thrombosis leads to total occlusion of blood flow, acute ST-elevation myocardial infarction (STEMI) is often the clinical outcome.

Given the primary role of thrombus in the genesis of acute coronary occlusion, the introduction of fibrinolytic therapy was a major advance in the treatment of STEMI. The net effect in major fibrinolytic trials was an approximate 30 percent reduction in the 7 to 10 percent short-term mortality(30 days).

Patients with acute STEMI should receive coronary reperfusion therapy with either primary percutaneous coronary intervention (PCI) or fibrinolysis as reperfusion improves clinical outcomes in nearly all groups of patients with STEMI who present within 12 hours of symptom onset.

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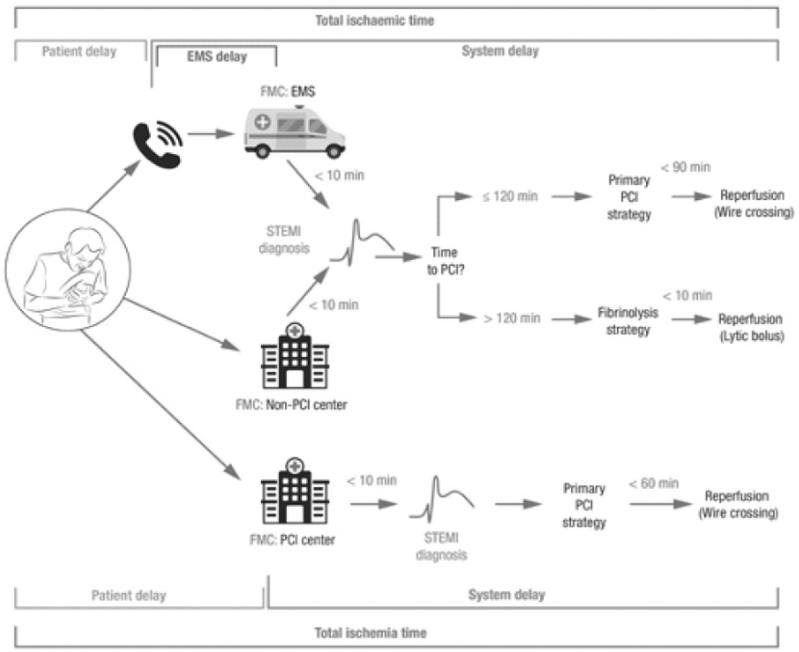
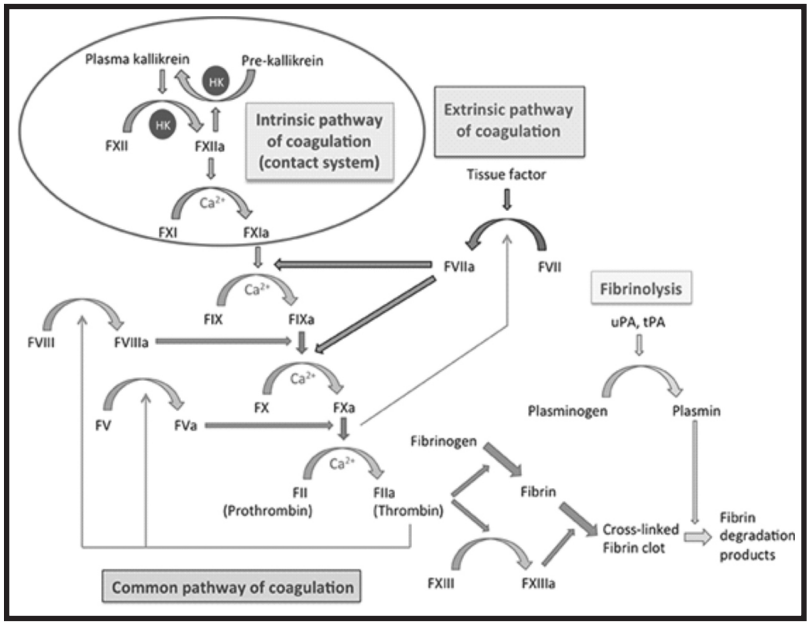
Based on data from various Trials including the DANAMI 2, PRAGUE 2 trials, Primary percutaneous coronary intervention (PCI) is preferred to Fibrinolytic therapy for most patients with ST elevation myocardial infarction (STEMI). However when timely primary PCI (more than 120 minutes) is not available, early fibrinolysis should be carried out.(ESC Guidelines).



HOW DOES FIBRINOLYTIC DRUG ACT



Currently used fibrinolytic drugs are intravenously infused plasminogen activators that activate the blood fibrinolytic system. These agents have a high specificity for their substrate plasminogen, hydrolyzing a peptide bond to yield the active enzyme plasmin. Free plasmin is rapidly neutralized by the serine proteinase inhibitor alpha-antiplasmin, whereas fibrin-bound plasmin is protected from rapid inhibition, thereby promoting clot lysis.

COMPARISON OF FIBRINOLYTIC AGENTS FOR TREATMENT OF STEMI

Characteristic	Streptokinase	Alteplase	Reteplase	Tenecteplase
Dose	1.5 MU	Up to 100 mg	10 U + 10 U	30–50 mg
Administration	Infusion (over 30 to 60 minutes)	Bolus and infusion (over 90 minutes)	Bolus (over 2 minutes) given 30 minutes apart	Bolus
Weight-based dosing	No	Yes	No	Yes
Antigenic	Yes	No	No	No
Patency rate[a]	60% to 68%	73% to 84%	84%	85%
Fibrin specificity[b]	No	Yes (++)	Yes (++)	Yes (++++)

a: 90-minute grade 2 or 3 TIMI blood flow
b: ++++ is stronger than ++
TIMI = Thrombolysis in Myocardial Infarction

CONTRAINDICATIONS — Absolute contraindications to fibrinolytic therapy include previous intracranial hemorrhage (ICH), known structural cerebral vascular lesion, known malignant intracranial neoplasm, ischemic stroke within three months, suspected aortic dissection, active bleeding or bleeding diathesis, or significant closed-head or facial trauma within three months.

Important relative contraindications include

Poorly controlled or chronic sustained hypertension (systolic blood pressure >180 mmHg)

• Ischemic stroke more than three months previously. Most patients with a history of a stroke were excluded from clinical fibrinolytic trials and, in clinical practice, are less likely to receive a fibrinolytic agent. Data evaluating such patients are extremely limited. In a review of 115 patients with acute myocardial infarction who had a prior nonhemorrhagic cerebrovascular event, 29 were given fibrinolytic therapy. None of the 29 had an intracranial bleed, and these patients had a lower one-year mortality than 46 patients with a prior stroke who did not receive a fibrinolytic agent (18 versus 33 percent).

• Dementia or other intracranial pathology (except as above).

• Traumatic or prolonged cardiopulmonary resuscitation (>10 minutes) or major surgery (within <3 weeks).

• Recent (within two to four weeks) internal bleeding.

• Noncompressible vascular puncture.

• For streptokinase: prior exposure (more than five days previously) or prior allergic reaction to these agents.

• Pregnancy

• Active peptic ulcer.

• Current use of anticoagulants: The higher the International Normalized Ratio, the higher the risk of bleeding.

• Increased risk of ICH. It has been suggested that fibrinolysis has a greater potential for harm than for benefit if the risk of ICH exceeds 4 percent. While the risk of ICH in patients is difficult to determine with certainty, the predictive model developed by the Cooperative Cardiovascular Project provides one method for making such an assessment. Patients with a score ≥ 5 according to this predictive model have a risk of ICH of 4.11 percent.

• Intraocular hemorrhage from fibrinolytic therapy in patients with diabetes mellitus is rare and diabetic retinopathy should not be considered a contraindication to fibrinolytic therapy in acute myocardial infarction.

LIMITATIONS OF FIBRINOLYSIS

• Despite the clear benefits of fibrinolytic therapy compared with no reperfusion and its ease of use, there are issues of both efficacy and safety that limit its use. The following limitations provided part of the impetus for primary percutaneous coronary intervention (PCI):

• The benefit of fibrinolysis is greatest when therapy is given within the first four hours after the onset of symptoms, particularly within the first **70 minutes** as the resistance of cross-linked fibrin to fibrinolysis is time-dependent Any longer delay decreases the amount of myocardial salvage and functional benefit. The absolute mortality benefit compared to placebo at five weeks is approximately 3 percent for those presenting within six hours from symptom onset, 2 percent for those presenting within 7 to 12 hours, and a nonsignificant 1 percent for those presenting within 13 to 18 hours. Unfortunately, many patients present to the hospital more than six hours after the onset of symptoms.

• Although patency, defined as some antegrade flow through the site of obstruction, is restored in up to 87 percent of infarct-related arteries, normalization of blood flow (as assessed by the TIMI flow grade) occurs in only 50 to 60 percent. The clinical benefits of fibrinolytic therapy correlate only with the restoration of normal (TIMI grade 3) flow. In contrast, TIMI grade 3 flow is achieved in 93 to 96 percent of patients who undergo primary PCI. Attainment of TIMI 3 flow is much more common with primary PCI: 93 to 96 percent in the PAMI and CADILLAC trials of more than 5400 patients.

• After apparently successful fibrinolysis, evidence of early recurrence of ischemia (pain or ST segment shifts) has been observed in 20 to 30 percent of patients with

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frank fibrinolytic coronary reocclusion in 5 to 15 percent, and reinfarction in 3 to 5 percent. Reinfarction is associated with higher rates of in-hospital, short-term, and long-term mortality.

• Major hemorrhagic complications occur in 2 to 3 percent. The most serious is intracerebral hemorrhage, which occurs in as many as 1 percent overall , 1.4 percent of older adults, and over 4 percent in patients with multiple risk factors . including Age More than 75 yrs, Female Sex Prior h/o Stroke, SBP > 160 mmhg Weight <65 Kgs for women and <80 Kgs for men, Prothrombin Time >24 and Use of Alteplase.

• As many as 20 to 30 percent of patients presenting with an acute STEMI, particularly older adults, are not candidates for fibrinolytic therapy because of contraindications such as active internal bleeding, a recent stroke, or hypertension.

• Efficacy of fibrinolytic therapy has not been demonstrated in patients in cardiogenic shock (unless coronary perfusion pressure is increased with an Intraaortic balloon pump [IABP]) or those with prior coronary artery bypass surgery (CABG).

• Fibrinolytic therapy does not necessarily involve early angiography, the findings of which may change treatment. In a report from the PAMI trial, 10 percent of patients who underwent angiography were considered inappropriate candidates for PCI due, in one-half of cases, to lack of residual stenosis that presumably reflected spontaneous clot lysis. Other patients have findings, such as severe three-vessel or left main coronary disease, or anatomic features unfavorable for PCI, that lead to a recommendation for surgical revascularization. Many experts now recommend routine angiography after fibrinolysis for those patients who have not had it performed for evidence of ongoing or recurrent ischemia.

To be continued in next issue

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