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Medi Quest BRS Hospital

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MYOCARDIAL INFARCTION

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

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Continuation of fibrinolysis of MI

USE IN SPECIFIC PATIENT GROUPS —

Although concerns have been raised about the use of fibrinolytic therapy in each of the following patient groups, the benefit outweighs the risk in most.

Elderly patients — Age, in the absence of other risk factors of adverse outcomes with fibrinolytic therapy, is not an absolute contraindication.

The mortality associated with STEMI treated with fibrinolytic therapy increases with increasing patient age, although fibrinolytic therapy still improves outcomes compared with placebo in older individuals . The frequency of left ventricular free wall rupture or major bleeding, and in particular intracranial hemorrhage, is higher in older patients treated with fibrinolytic therapy.

In the STREAM trial that evaluated a pharmacoinvasive strategy (fibrinolysis with tenecteplase followed by rescue or elective percutaneous coronary intervention [PCI] within 24 hours), the incidence of intracranial hemorrhage was significantly reduced when elderly patients received half the dose of the fibrinolytic agent. This strategy has not been well studied.

Cardiogenic shock — In patients with cardiogenic shock, there is a strong preference for primary PCI rather than fibrinolytic therapy. However, for patients who cannot receive timely primary PCI, fibrinolysis followed by PCI, even if there is a delay of up to 24 hours, is the preferred strategy. This is especially the case if the patient presents early (<3 hours) after symptom onset.

Prior MI — Although patients with a prior MI did not appear to benefit from fibrinolysis in GISSI-2 , other trials have noted a reduction in mortality from fibrinolytic therapy.

Prior CABG — Patients with prior coronary artery bypass graft surgery (CABG) occasionally present with an acute STEMI (4 percent in GUSTO-I). The infarct-related artery in these patients was more likely to be a native coronary artery than a bypass graft (62 versus 38 percent). The outcome of fibrinolytic therapy in these patients was evaluated in the (United States) National Registry of Myocardial Infarction 2, in which 6.4 percent of almost 40,000 patients treated with alteplase had had a prior CABG. Prior CABG was an independent predictor of mortality with a multivariate analysis (odds ratio 1.23). There was no difference in outcome between reperfusion therapy using primary PCI or a fibrinolytic agent.

Menstruating women — Some practitioners are concerned about the use of fibrinolytic agents in menstruating women. Among 12 menstruating women in GUSTO-I, there was no significant increase in severe bleeding compared with nonmenstruating women. There was a significant increase in moderate bleeding that was offset by the benefits of fibrinolytic therapy.

Diabetes mellitus — Diabetes mellitus is associated with increased mortality in the setting of an acute MI. In GUSTO-I, the approximately 15 percent of patients with diabetes had a similar benefit from fibrinolysis but a significantly higher

mortality rate at 30 days (11.3 versus 5.9 percent) and one year (14.5 versus 8.9 percent) than patients without diabetes. One possible explanation could be a higher incidence of unsuccessful reperfusion, as evaluated by resolution of ST-segment elevation in diabetic patients after fibrinolysis.

INITIATION OF THERAPY — For patients with ST elevation myocardial infarction (STEMI) in whom fibrinolysis is chosen as the reperfusion strategy (ie, when primary percutaneous coronary intervention is not available), treatment should be given as soon as possible after the diagnosis.

Prehospital fibrinolysis — Administration of fibrinolytic therapy before hospital arrival (eg, in an ambulance) for acute STEMI is an established practice in many countries. The rationale is to shorten the time between the onset of symptoms and the restoration of coronary blood flow in the occluded artery.

A 2000 meta-analysis of six randomized trials (6434 patients) comparing prehospital with in-hospital fibrinolysis found:

☒Shorter time to fibrinolysis (104 versus 162 minutes)

☒Reduced all-cause hospital mortality (odds ratio 0.83, 95% CI 0.70-0.98).

Similar findings were noted in a 2014 meta-analysis.

Timing — Based on observations from randomized trials and from real world settings, the time from hospital arrival to drug administration (door-to-needle time) should be less than 30 minutes.

In patients with an acute STEMI, fibrinolytic therapy should not await the availability of results of cardiac biomarkers.

A mortality benefit is less likely with fibrinolytic therapy at 13 to 18 hours. A meta-analysis from the Fibrinolytic Therapy Trialists' Collaborative Group found that the absolute mortality benefit from fibrinolytic therapy at five weeks was 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 .

However, there may be benefit in patients presenting 12 hours after symptom onset and possibly up to 24 hours if the patient has ongoing or stuttering chest pain. Although most myocardial necrosis occurs early (within the first 90 to 180 minutes), the advantages of late reperfusion are presumably related to the presence of a patent infarct-related vessel, leading to improved ventricular healing, reduced infarct expansion, and greater electrical stability.

CONCOMITANT THERAPIES — All ST elevation myocardial infarction (STEMI) patients receiving fibrinolytic therapy should receive the following therapies as soon as possible in the emergency department.

Anticoagulant therapy — STEMI patients receiving fibrinolytic therapy should be treated with an anticoagulant. It should be started as soon as a decision to treat with fibrinolytic therapy is made.

In these patients, who will likely receive percutaneous coronary intervention (PCI) after fibrinolytic therapy, prefer unfractionated heparin. For patients receiving fibrinolysis, an intravenous bolus of 60 to 100 units/kg (maximum of 4000 units) followed by 12 units/kg/hour (maximum 1000 units/hour) intravenously to achieve an activated partial thromboplastin time of 50 to 70 seconds. For patients who will not receive PCI after fibrinolysis, Low Molecular Weight Heparin is prefered.

Antiplatelet therapy — aspirin (loading dose of 162 to 325 mg of uncoated aspirin) is given as soon as possible after the diagnosis has been made.

Once fibrinolysis is chosen as the reperfusion strategy, a P2Y12 receptor blocker to all patients (Clopidogrel, Ticagrelor)

Statins — For all patients with an acute coronary syndrome not on treatment with a statin, initiate high-intensity statin therapy (80 mg of atorvastatin or 20 to 40 mg of rosuvastatin daily) regardless of the baseline low density lipoprotein-cholesterol level

Beta blocker — For all patients with acute MI, start oral beta blockers within the first 24 hours, as long as no contraindications are present.

COMPLICATIONS — Bleeding is the primary complication of fibrinolytic therapy, and hemorrhagic stroke is the greatest concern. These events modestly reduce the total benefit associated with fibrinolytic therapy.

In addition, allergic reactions can be seen in patients treated with streptokinase.

Bleeding — GUSTO-I, the largest trial of fibrinolytic therapy (streptokinase or alteplase), found a 1.8 percent incidence of severe bleeding . The incidence of moderate bleeding, defined by the need for transfusion but without hemodynamic compromise or need for an intervention, was 11.4 percent. Bleeding was most often procedure related, occurring with coronary artery bypass graft in 3.6 percent, and at the groin site of a percutaneous coronary intervention in 2 percent. As the use of the radial artery for access has increased, the risk of significant procedure-related bleeding has decreased.

The most common site for spontaneous bleeding is the gastrointestinal tract (1.8 percent) . The risk of moderate or severe bleeding appears to be greater in women than men (odds ratio 1.43).

Stroke — The risks of stroke and intracranial hemorrhage (ICH) were 1.2 and 0.7 percent in a non-trial community registry of 12,739 patients . In GUSTO-I, the majority of strokes (95 percent) occurred within five days of therapy .The incidence was somewhat higher with alteplase.

Strokes associated with fibrinolysis are associated with a very high rate of mortality and morbidity. In GUSTO-I, the stroke was fatal in 41 percent and produced moderate or severe disability in 31 percent . Similar findings were noted in the (United States) National Registry of Myocardial Infarction-2 registry.

Risk factors for stroke have been identified from analysis of patients enrolled in randomized trials .In GUSTO-I, patients with a previous transient ischemic attack or stroke were at particularly high risk (5.5 and 6.9 percent, respectively)

☒ Independent predictors of ICH included the following:
☒ Age ⩾75 years
☒ Black race
☒ Female sex
☒ Prior history of stroke
☒ Systolic blood pressure ⩾160 mmHg
☒ Weight ⩽65 kg for women or ⩽80 kg for men
☒ International Normalized Ratio >4 or prothrombin time >24 seconds
☒ Use of alteplase (versus other fibrinolytic agent)

☒ ICH should be suspected in any patient who develops sudden neurologic deterioration, a decline in level of consciousness, new headache, nausea and vomiting, or a sudden rise in blood pressure after fibrinolytic therapy, especially within the first 24 hours of treatment. The management of such patients is similar to that for patients with ICH of any cause.

MANAGEMENT AFTER FIBRINOLYSIS — For stable patients, referral for diagnostic angiography and percutaneous coronary intervention (PCI) compared with a strategy of medical therapy, based on evidence of better outcomes with the former. This recommendation includes patients with minimal increase in troponin.

Successful reperfusion is generally associated with significant improvement in ischemic symptoms, resolution of ST-elevation on the electrocardiogram, hemodynamic stability, and the absence of heart failure. For the patient who has responded to fibrinolytic therapy, an important issue is the role of subsequent coronary angiography and revascularization.

For the patient with evidence that reperfusion has been unsuccessful (failed fibrinolysis), immediate angiography with an intent to perform rescue percutaneous intervention is recommended .

Primary failure of fibrinolysis is often manifested clinically by persistent or worsening chest pain (particularly if associated with other symptoms such as dyspnea and diaphoresis), persistent or worsening ST segment elevation, and/or hemodynamic instability or heart failure. However, these clinical factors are not sufficiently predictive in all patients. As a result, in the absence of clear indications of reperfusion, the clinician must maintain a high index of suspicion for primary failure.

A pharmacoinvasive strategy has been proposed. In the STREAM trial , the time to reperfusion with fibrinolysis (tenecteplase) was shortened and patients were referred to a percutaneous coronary intervention (PCI) center for elective or rescue PCI. With this strategy, patients treated with early fibrinolysis or primary PCI had a similar incidence of adverse outcomes at 30 days. Moreover, only 36 percent of patients underwent rescue PCI and 64 percent had an elective coronary angiogram and PCI within 24 to 48 hours. Persistence of symptoms or lack of ST segment resolution should prompt rescue PCI.

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