Cardiac Diseases and Therapies
ACUTE CORONARY SYNDROMES
GUIDELINES FOR FIBRINOLYSIS

Early systemic fibrinolysis has been shown to reduce mortality in patients presenting with an acute coronary occlusion. Although primary PCI is generally a preferred strategy, systemic fibrinolysis should be considered when there will be a significant delay to primary PCI, or when primary PCI is not available.

INDICATIONS FOR FIBRINOLYSIS

1. PERSISTENT symptoms of acute coronary occlusion at rest ***and***
   PERSISTENT ECG indicators of a transmural current of injury defined by:
   - ST segment (80 ms past J point) elevation >1 mm in 2 contiguous limb leads ***or***
   - ST segment elevation >2 mm in 2 contiguous precordial leads ***or***
   - Left Bundle Branch Block (LBBB) may mask the ECG indications of an acute coronary occlusion. In patients with chest pain and a LBBB clinical judgement may identify the subset of patients that have an acute coronary occlusion, and that may benefit from a patency intervention.
2. Patient presentation within 6 hours of persistent coronary occlusion:
   Note: Fibrinolytic therapy could be considered in patients presenting 7 to 12 hours after onset of symptoms if there is a reasonable chance that the artery may have been occluded less than 6 hours.
3. When fibrinolytic therapy is indicated, it should be started as soon as possible after presentation. This will require a process to facilitate rapid triage, rapid diagnosis and decision to treat, and the prompt delivery of fibrinolytic therapy.
4. Fibrinolytic therapy produces a risk of hemorrhage and clinical instability. The risk to benefit ratio must be considered carefully for each patient. In most patients the benefits of fibrinolytic therapy outweigh the risks. The most serious bleeding risk in most patients is intracranial hemorrhage (see warnings below).

CONTRAINDICATIONS FOR FIBRINOLYSIS

- Active bleeding or bleeding diathesis (except menstrual bleeding)
- History of hemorrhagic stroke
- History of cerebrovascular event within 3 months
- Intracranial or intraspinal surgery or trauma within 3 months
- Intracranial neoplasm (primary or metastatic, arteriovenous malformation or aneurysm)
- Suspected aortic dissection

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WARNINGS FOR FIBRINOLYSIS

A. The following factors have been associated with an increased risk of intracranial hemorrhage:
- Age >65 years
- SBP>180 or DBP >110 (highest recorded in ED)
- Female gender
- Body weight <60 kg
- Remote CNS pathology

B. In the following situations, the risk of therapy may be increased and should be weighed against the anticipated benefits:
- Recent trauma (2-4 weeks) including head trauma
- Traumatic or prolonged (>10 minutes) CPR
- Recent major surgery (2-4 weeks)
- Cerebrovascular disease >3 months or dementia
- Pregnancy
- Diabetic hemorrhagic retinopathy or other hemorrhagic ophthalmic conditions
- Active peptic ulcer disease
- Non-compressible vascular punctures
- Patients currently receiving oral anticoagulants or with a bleeding diathesis

PRECAUTIONS FOR FIBRINOLYSIS

- Minimize vascular punctures
- No intramuscular injections
- Avoid non-compressible sites for central IV access (i.e. jugular, subclavian)
- Avoid invasive monitoring if possible within the first 6 hours post-fibrinolysis
- Avoid invasive pacing if possible within the first 6 hours post-fibrinolysis
- Caution with automatic blood pressure cuff as it may cause a forearm hematoma
- Use saline lock for drawing blood

ADVERSE EFFECTS OF FIBRINOLYSIS

- Bleeding
- Reperfusion arrhythmias (highest incidence within the first 24 hours)
- There may be an increased risk of ventricular rupture and hemorrhagic pericarditis

GUIDELINES FOR FIBRINOLYSIS

TREATMENT PROTOCOL

Orders should be initiated for the following:

- Admission to a critical care area (CICU)
- IV access with two IV lines: 18 gauge saline lock in one arm (for TNK) **AND** 20 gauge angiocath in the opposite arm with 250 mL D5W to keep vein open
- Baseline investigations: CBC, INR, aPTT, electrolytes, creatinine, CK, troponin q8h x 48 hours
- Continuous ECG monitoring
- Urinalysis
- Portable chest x-ray
- All potential bleeding sites should be observed closely: Generalized assessment for bleeding q1h x 6 then q2h x 6 then q4h x 48 hours

A. FIBRINOLYTIC REGIMENS FOR ACUTE CORONARY OCCLUSION

1. Tenecteplase

1) Reconstitute 50 mg of tenecteplase using the supplied syringe and diluent vial. This will give a final concentration of 5 mg/mL.
2) Administer as a **single bolus** over 5 seconds through saline lock.

Patient Weight (kg)	Tenecteplase Dose (mg)	Volume (mL)
<60	30	6
≥60 to <70	35	7
≥70 to <80	40	8
≥80 to <90	45	9
≥90	50	10

Note: *The total dose does not exceed 50 mg*

B. ADJUVANT REGIMENS

1. Antiplatelet Agents

- **Acetylsalicylic acid (ASA)** 160 mg orally to chew as soon as possible after clinical impression of evolving AMI.
  Continue ASA EC 81mg orally once daily indefinitely.

- **Clopidogrel** 300mg x1 orally as loading dose (consider omitting loading dose if age greater than 75 years), followed by Clopidogrel 75mg orally once daily as a maintenance dose

2. Anticoagulants

Unfractionated Heparin (IV)

- Give a bolus of unfractionated heparin 60 units/kg (maximum 4,000 units) IV at the time of tenecteplase administration, then infuse unfractionated heparin (using 25,000 units/250 mL D5W bag) at 12 units/kg/h (maximum 1000 units/h) IV for 48 hours.
- Please refer to Heparin Intravenous Orders (Form 3313) – LOW Target Heparin nomogram for aPTT titration and monitoring.
- Continuation of unfractionated heparin beyond 48 hours should be undertaken for recurrent ischemia and conversion to oral anticoagulation should be strongly considered in the presence of high risk factors for systemic or venous thromboembolism (e.g. prior embolus, atrial fibrillation).
- Systemic thrombolysis is generally administered with effective anti-thrombin therapy. Systemic thrombolysis may be given to patients on maintenance anticoagulants, although patients on warfarin with an INR greater than 3 have a higher risk of major bleeding. Although there is less experience with the direct oral anticoagulants, the dose response is more predictable than with warfarin. In patients on oral anticoagulants, heparin should be delayed to an expected tapering of the effect of the maintenance anticoagulants.

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REFERENCES

1. University Health Network and Mount Sinai Hospital Management of ST Elevation Acute Coronary Syndromes Pocket Card Revised June 2006.
2. O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines [published correction appears in Circulation. 2013 Dec 24;128(25):e481]. Circulation. 2013;127(4):e362-e425.
3. Van De Werf F, Adgey J, Ardissino D, et al. Single-bolus tenecteplase compared with front-loaded alteplase in acute myocardial infarction: the ASSENT-2 double-blind randomised trial. Lancet. 1999;354(9180):716-22.
4. ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2. Lancet. 1988;2(8607):349-60.
5. Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO III) Investigators. A comparison of reteplase with alteplase for acute myocardial infarction. N Engl J Med. 1997;337(16):1118-23.
6. Granger CB, Hirsch J, Califf RM, et al. Activated partial thromboplastin time and outcome after thrombolytic therapy for acute myocardial infarction: results from the GUSTO-I trial. Circulation. 1996;93(5):870-8.
7. TIMI Study Group. Comparison of invasive and conservative strategies after treatment with intravenous tissue plasminogen activator in acute myocardial infarction. Results of the thrombolysis in myocardial infarction (TIMI) phase II trial. N Engl J Med. 1989;320(10):618-27.
8. Chen ZM, Jiang LX, Chen YP, et al. Addition of clopidogrel to aspirin in 45,852 patients with acute myocardial infarction: randomised placebo-controlled trial. Lancet. 2005;366(9497):1607-21.
9. Yusuf S, Mehta SR, Chrolavicius S, et al. Effects of fondaparinux on mortality and reinfarction in patients with acute ST-segment elevation myocardial infarction: the OASIS-6 randomized trial. JAMA. 2006;295(13):1519-30.
10. Antman EM, Morrow DA, McCabe CH, et al. Enoxaparin versus unfractionated heparin with fibrinolysis for ST-elevation myocardial infarction. N Engl J Med. 2006;354(14):1477-88.
11. Sabatine MS, Cannon CP, Gibson CM, et al. Addition of clopidogrel to aspirin and fibrinolytic therapy for myocardial infarction with ST-segment elevation. N Engl J Med. 2005;352(12):1179-89.

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