Antiplatelets in ACS

Jasmine Jeyarajah
Department of Cardiology
Sheba

Overview

- Definition of ACS
- UA, NSTEMI and STEMI
- Management
- Role of antiplatelets
- Guidelines

Acute Coronary Syndrome (ACS)

Definition: a constellation of symptoms related to obstruction of coronary arteries with chest pain being the most common symptom in addition to nausea, vomiting, diaphoresis etc.

Chest pain concerned for ACS is often radiating to the left arm or angle of the jaw, pressure-like in character, and associated with nausea and sweating. Chest pain is often categorized into typical and atypical angina.

Unstable angina

- Occurs at rest and prolonged, usually lasting >20 minutes
- New onset angina that limits activity
- Increasing angina: Pain that occurs more frequently, lasts longer periods or is increasingly limiting the patients activity

Non ST Elevation MI

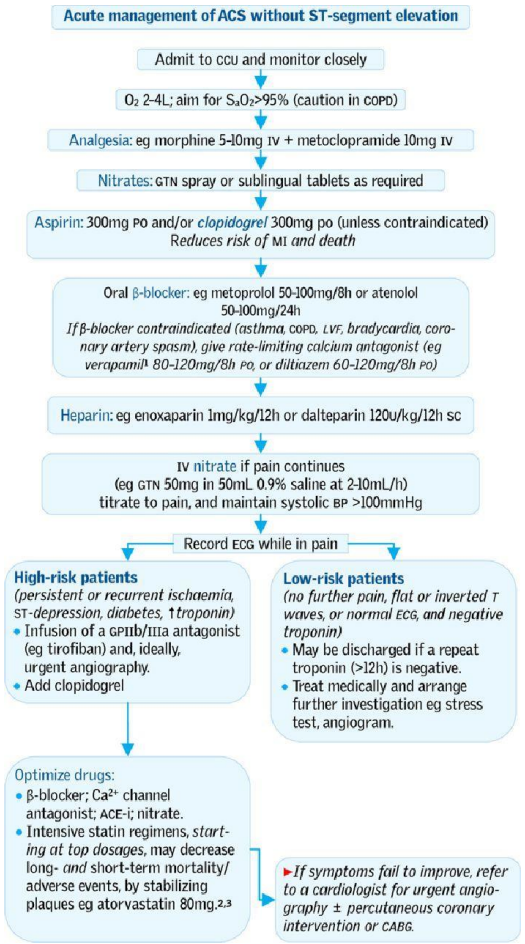
- Common mechanism to all ACS is rupture/erosion of fibrous cap of a coronary artery plaque.
- This → platelet aggregation & adhesion, localized thrombosis, vasoconstriction & distal thrombus embolization
- ECG changes:
  - ST depressions (0.5 mm at least) or T wave inversions (1.0 mm at least) without Q waves in 2 contiguous leads with prominent R wave.
  - Isolated T wave inversions:
    - can correlate with increased risk for MI
    - may represent Wellen's syndrome:
      - critical LAD stenosis
      - >2mm inversions in anterior precordial leads

ST Elevation MI

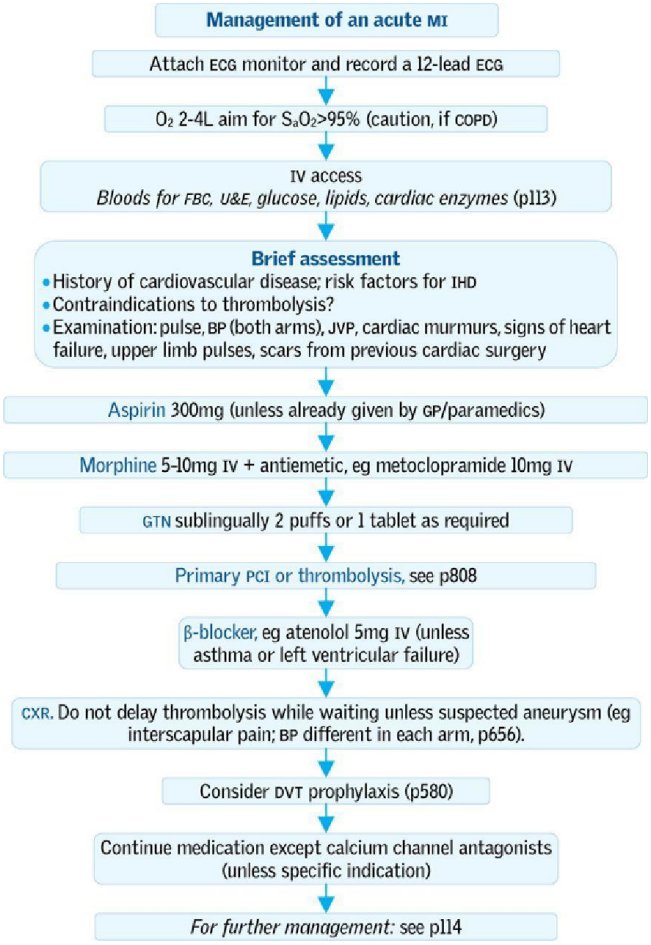
- Rupture/erosion of vulnerable coronary artery plaque can → prolonged occlusion of a coronary artery → myocardial necrosis in 15-30 mins
- Subendocardial myocardium initially affected but
  - **Continued** ischaemia infarct zone extends through to subepicardial myocardium → **transmural** Q wave MI.
- ECG changes:
  - Q waves , ST elevations, hyper acute T waves; followed by T wave inversions.
  - Clinically significant ST segment elevations:
    - > than 1 mm (0.1 mV) in at least two anatomical contiguous leads
    - or 2 mm (0.2 mV) in two contiguous precordial leads (V2 and V3)

ACUTE Management!

NSTEMI



STEMI



ANTIPLATELET Therapy

- Includes:
  - Aspirin
    - Caution: if pt has active peptic ulcers
  - Clopidogrel
    - Caution: if pt at inc risk of bleeding (CABG plan)
  - Prasugrel
  - Ticagrelor
    - (oral reversible P2Y12 antagonist)

Platelets and Antiplatelet therapy

- Platelets are a key component in thrombosis cascade in ACS
- Rupture of atheromatous plaque exposes circulating platelets to:
  - ADP (adenosine diphosphate), thromboxane A2 (TxA2), adrenaline, thrombin and collagen tissue factor.
    - This →**platelet activation**, with thrombin as an especially potent stimulant of such activity.
    - Platelet activation→ stimulates expression of **glycoprotein (GP) IIb/IIIa receptors on platelet surface**.
      - These receptors **bridge fibrinogen between adjacent platelets → platelet aggregation.**

Antiplatelet therapy

- ASPIRIN
  - **Aspirin blocks the formation of thromboxane A2 and so**
  - prevents platelet aggregation. In ACS patients, 75–150 mg aspirin ↓ relative risk of death or myocardial infarction by about 35–50%.

Antiplatelet therapy

- CLOPIDOGREL
  - **Is a thienopyridine that inhibits ADP dependent activation of the GPIIb/IIIa complex that allows platelet aggregates to form.**
  - However, *clopidogrel is a pro-drug* requiring conversion by hepatic cytochrome P450 enzymes to an active moiety that binds irreversibly to $P2Y_{12}$ receptor on platelet membranes and inhibits ADP dependent pathway of platelet activation.
  - PPI's, e.g. *omeprazole, and genetic variation in the* cytochrome P450 enzymes may theoretically ↓ effectiveness of clopidrogel.
    - This has not been a problem in clinical practice.

Antiplatelet therapy

- ***Activated GP (glycoprotein) IIb/IIIa receptors on platelets***
  - **Bind to fibrinogen initiating platelet aggregation.**
  - **Receptor antagonists** have been developed that are powerful **inhibitors** of platelet aggregation.
  - Abciximab is a monoclonal antibody that binds tightly and has a long half-life.
  - Eptifibatide is a cyclic peptide that selectively inhibits GPIIb/IIIa receptors, but has a short half-life and wears off in 2–4 h.
  - Tirofiban is a small non-peptide that rapidly blocks the GPIIb/IIIa receptors and is reversible in 4–6 h.

Guidelines

- Guidelines from European Society of Cardiology (ESC)[3] and American College of Cardiology and American Heart Association (ACC/AHA)[4] recommend:
  - In **STEMI**:
    - Routine use of aspirin ASAP after onset of symptoms of acute MI & as **lifelong therapy thereafter**.
    - Clopidogrel is recommended as an alternative in patients who cannot tolerate aspirin
  - In **NSTEMI**:
    - Aspirin ↓ death & MI in patients with UA or NSTEMI and is associated with a ↓ incidence of adverse effects
    - Aspirin - recommended as **acute & long-term treatment** for all patients with NSTE-ACS unless it is contraindicated

THE END