Cardiology Update

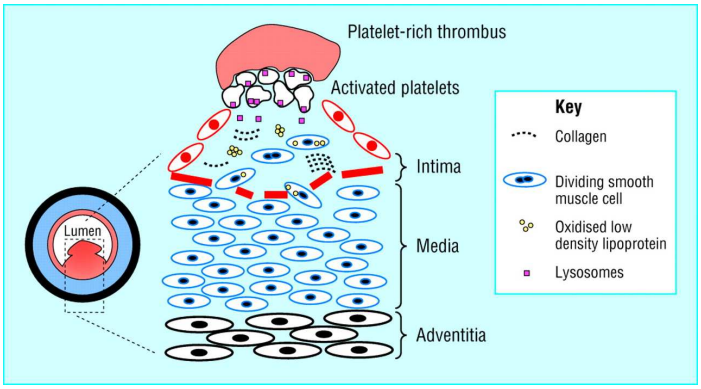
Michelle Cerrato
Lead Cardiovascular and Thoracic Pharmacist

SUHT November 2009

Acute Coronary Syndromes (ACS)

- ACS refers to a range of acute myocardial ischaemic states.
  - unstable angina
  - non-ST segment elevation myocardial infarction (NSTEMI)
  - ST segment elevation myocardial infarction (STEMI)
- Thrombus formation on an atheromatous plaque and then disruption of that thrombus causes ACS.
- If untreated, the prognosis is poor and mortality high
- Appropriate triage and timely use of acute interventions (invasive or pharmacological) are vital

Diagram of an Unstable Plaque



Grech, E. D et al. BMJ 2003;326:1259-1261

bmj.com

Plan for Session

- Quiz
- Quick overview of current guidelines
- Case study
- Questions

Quiz

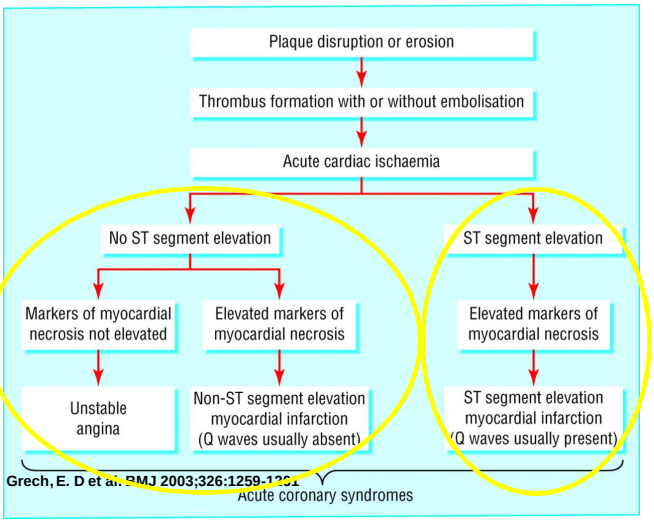
Quiz Answers

Drug	Mechanism of Action	Side Effect
Ranolazine	Inhibits Na overload in myocytes	Dizziness
Ivabradine	If channel inhibitor in SAN	Affects the visual field
Ramipril	Inhibits ACE	Renal impairment
Bisoprolol	Beta receptor antagonist	Fatigue
Doxazosin	Alpha antagonist	Hypotension
Prasugrel	ADP receptor antagonist	Bleeding
Enoxaparin	Activates antithrombin III to inhibit factors Xa and IIa	Thrombocytopenia
Fondaparinux	Activates antithrombin III to inhibit factor Xa only	Bleeding
Simvastatin	HMG co-A reductase inhibitor	Myopathy

Treatment of NSTEMI

- Treatment of ACS has rapidly developed over last 10 years
- Platelet aggregation and thrombus formation play a key role in ACS
- Advances in treatment such as the GP IIb/IIIa inhibitors, LMWH, anti-thrombin agents and clopidogrel, and the more widespread use of PCI raise questions about optimal management - addressed with NICE ACS guideline, currently draft and out for consultation

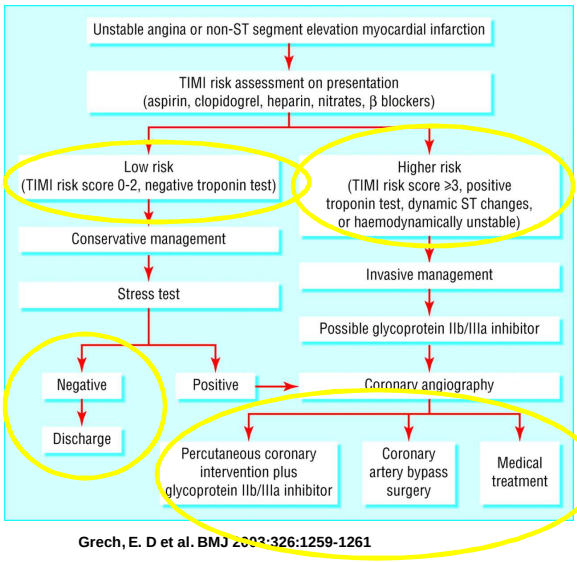
Spectrum of Acute Coronary Syndromes



Grech, E. D et al. BMJ 2003;326:1259-1261

bmj.com

Treatment of UA and NSTEMI ACS



Grech, E. D et al. BMJ 2003;326:1259-1261

bmj.com

Current NSTEMI Management at SGH

- Aspirin
- Clopidogrel
- Enoxaparin 1mg/kg BD
- Statin – simvastatin 40mg OD first line, higher intensity statin in some cases
- ACEi
- Beta-blocker
- SBCA ⇒ stenting as appropriate
- Also test for ischaemia

What is a STEMI?

- A STEMI is the most severe type of ACS
- A coronary artery suddenly becomes completely blocked by a blood clot, causing virtually all the heart muscle to start to die.
- Determined on ECG shown as ST segment elevation
- ST elevation indicates that a relatively large amount of heart muscle damage is occurring

STEMI at SUHT

- 24 hours a day pPCI service
- Aspirin and clopidogrel loading
- IV heparin
- GpIIb/IIIa inhib or thrombin inhibitor as part of pPCI
- MI secondary prevention medication (as per g/l)
- Discharged day 3 usually
- Thrombolysis now only given very occassionally
- Planned development - use of prasugrel

NICE ACS Guideline (Draft July 2009)

- Key recommendations:
  - Offer coronary angiography within 96 hours of first admission to hospital (patients at intermediate or high risk of further events)
  - Ischaemia testing
  - Advice and information on discharge
- **Treatment recommendations:**
  - Aspirin – loading + maintenance dose
  - Clopidogrel – loading + maintenance dose, continue for 1 year
  - IV tirofiban or eptifibatide for intermediate or high risk patients
  - Antithrombin agent in patients not at high risk of bleeding
  - Consider IV heparin as an alternative in patients with sig. renal impairment
  - Do not use bivalirudin for the routine management of NSTEMI

NICE G/L MI Secondary Prevention [no. 48] – applies to all ACS patients

- TTO should include diagnosis, results of investigations, future management plans and advice on secondary prevention
- Physically active for 20–30 minutes a day to the point of slight breathlessness
- Stop smoking advice
- Eat a Mediterranean-style diet
- Cardiac rehabilitation should be equally accessible and relevant to all patients
- All patients should be offered treatment with a combination of:
  - ACE inhibitor, beta-blocker, aspirin and statin
- Patients post-acute MI with symptoms of heart failure and LVSD should be given eplerenone, initiated within 3–14 days of the MI
- Clopidogrel + low-dose aspirin for 12 months after NSTEMI, and 4 weeks after STEMI (12 months if have a stent)
- All patients should be offered a cardiological assessment to consider whether coronary revascularisation is appropriate. This should take into account co-morbidity

NICE Lipid G/L [no. 67] – Secondary Prevention

- Start treatment straight away
- Statin therapy is recommended for adults with clinical evidence of CVD
  - Start with simvastatin 40mg OD – consider interactions and patient factors
  - Consider increasing to simvastatin 80 mg or similar if TC< 4 mmol/L or LDL-c <2 mmol/L is not attained
- People with ACS should be treated with a higher intensity statin.
- If statins are not tolerated consider fibrates, nicotinic acid, anion exchange resins or ezetimibe

Prasugrel

- NICE technology appraisal Sept 2009
- Recommended for use in:
  - immediate pPCI for STEMI
  - Patients with ACS who have had stent thrombosis during clopidogrel treatment
  - Patients with diabetes mellitus going for PCI
- Prasugrel is an oral inhibitor of platelet activation and aggregation through the irreversible binding to ADP receptors on platelets.
- Main advantages of prasugrel over clopidogrel are faster antiplatelet action and less variable response.
- Main disadvantage: prasugrel increased the chance of potentially fatal bleeding compared with clopidogrel

Other New Medication

- **Ivabradine**
  - Treatment of angina in patients in SR
  - Ivabradine selectively inhibits I*f* channels in the sinoatrial node, to reduce cardiac pacemaker activity and slow heart rate
  - Used when beta-blockers fail or are not tolerated (BEAUTIFUL study)
  - Ivabradine + betablockers - The ASSOCIATE study
  - Do not give if HR < 60 beats per minute
  - Eye effects, bradycardia, interactions with CYP3A4 inhibs
- **Ranolazine**
  - New class of antianginal
  - Inhibits intracellular sodium overload in the myocytes in the cardiac muscle causing improved myocardial relaxation
  - Minimal effects on HR and BP
  - For patients already on maximal anti-anginal therapy that they can tolerate who are not suitable for further intervention but are experiencing angina symptoms
  - Well tolerated, can prolong QT
  - C/I: severe renal imp., moderate liver imp.
  - Interactions: potent CYP3A4 inhibitors + can't use with some anti-arrhythmics
  - S/E: dizziness, nausea

Case Study

Case Study Answers (1)

1. Load with aspirin and clopidogrel, IV GTN?, oxygen, analgesia/antiemetic, enoxaparin, insulin sliding scale, stop bendroflumethiazide and amlodipine
2. Betablocker& ACEi – shown to reduce mortality post ACS in various trials, statin – platelet stabilising? + reduce cholesterol (suggest high intensity statin), stop smoking, reduce alcohol intake, Mediterranean diet
3. Clopidogrel and omeprazole theoretical interaction but now disputed

Case study Answers (2)

4. Change to prasugrel, 60mg loading then possibly 5mg OD as >75yrs so higher risk of bleeding
5. Amiodarone 300mg over 1 hour, then 900mg over 23 hours IV via a central line ideally, administer in 500ml glucose 5%
6. If continue on amiodarone may need to reduce simvastatin dose prescribed or change to atorvastatin.

   If manage AF with a betablocker then no interactions with other medication

   If give digoxin, monitor levels 6 hours post dose, used for rate control in chronic fast AF.

   Potentially may need warfarin as high stroke risk but already on prasugrel + aspirin so probably not until prasugrel course finished, ok to use aspirin and warfarin combination

Summary

- Lots of new NICE guidelines for ACS patients
- New things for SUHT
  - Fondaparinux?
  - Bivalirudin
  - Prasugrel
  - High intensity statins
- Some other new drugs currently available and being reviewed

Any Questions?