ACUTE CORONARY SYNDROMES

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Definitions & Epidemiology

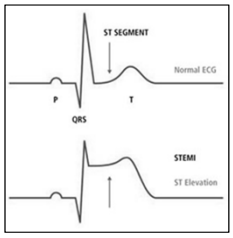
- ACS includes STEMI, NSTEMI, and unstable angina (UA)
- ECG differentiates STEMI from NSTEMI/UA
- ACS is the leading cause of death from CVD
- In the year following AMI, 23% of women and 18% of men will die, most likely from recurrent infarction
- 2/3 of ACS is NSTEMI/UA, 1/3 is STEMI
- Mortality rates of STEMI and NSTEMI are similar at 1 yr

Pathophysiology

- Review formation of atherosclerotic plaque in SIHD notes
- Smaller plaques are more likely to cause ACS
- ACS results from rupture of atherosclerotic plaque and subsequent initiation of clotting cascade. A clot is formed that consists of platelets and fibrin
- The resulting degree of coronary blockage and myocardial necrosis determines diagnosis

Pathophysiology
STEMI

- Also called Q-wave MI
- Usually results from fibrin-rich "red" clot that fully occludes a coronary artery
- Causes necrosis of myocardial tissue which appears as ST elevation
- Injury is usually full-thickness of myocardium



Pathophysiology
STEMI/UA

- NSTEMI/UA usually result from platelet-rich "white" clot that incompletely occludes a coronary artery and cause significant ischemia and possibly partial-thickness injury to myocardium
- ST depression or no change is seen on ECG
- NSTEMI is also called non-Q wave MI

Pathophysiology
Ventricular Remodeling Post-MI

- Initiates after an infarction, changes the shape, function, and size of the ventricle
- Ultimately leads to heart failure
- Various factors cause it, including neurohormonal remodeling (RAAS and SNS activation), mechanical factors, hemodynamic factors, and changes in gene expression

Presentation of ACS

- Symptoms
  - Acute distress with chest discomfort lasting >20 min
  - More intense and longer duration than stable angina
  - Pain may radiate to arm, back, or jaw
  - Can be accompanied by N/V, SOB
- Signs
  - Acute heart failure
  - Arrhythmias

Presentation of ACS

- Labs
  - Heart enzymes (troponin and CK-MB)
  - Blood chemistry for electrolytes and SCr
  - CBC, aPTT, INR
  - Labs for assessing risk factors and co-morbidities

Presentation of ACS

- 12-Lead ECG
  - Key in diagnosing ACS
  - Obtained within 10 min of suspicious presentation
  - Look for ST and T-wave, correlate with enzymes
  - Identifies the location of the coronary artery causing ischemia/infarction

Risk Stratification

- ST Elevation
  - Presumed STEMI
  - Highest risk for death
  - Reperfusion has highest chance to increase survival
- NSTEMI/UA
  - Lower risk for death
  - Risk stratification according to TIMI score
  - According to risk may proceed with PCI or more conservative therapy

Non-Pharmacologic Treatment

- PCI for STEMI
  - Early reperfusion is most effective option within 12h of symptom onset
  - PCI should be performed within 90 minutes of presentation (door-to-balloon time)
  - If PCI unavailable or delayed beyond 90 min then fibrinolytic therapy should be administered instead
  - If > 12h from symptom onset, PCI or CABG are options
  - Treatment should be timely: door-to-needle time < 30 min, door-to-balloon time < 90 min
  - PCI is generally safer and more effective than fibrinolytics
- PCI or CABG for NSTEMI/UA
  - Rec'd for pts with moderate-high risk NSTEMI/UA

Early Pharmacologic Therapy (ED)
All STEMI

- Oxygen: if O2 sats < 90%
- Nitroglycerin: SL x 3 for all pts. if necessary. Follow with IV NTG in pts with ongoing discomfort, HTN, or pulmonary congestion
- Aspirin (162-325 mg) and $P2Y_{12}$ Inhibitor (clopidogrel, prasugrel, ticagrelor)
- Anticoagulant (UFH, enoxaparin, fondaparinux, or bivalirudin)
- Fibrinolytic therapy if PCI not performed

Pharmacologic Therapy
STEMI and PCI: Antiplatelet

- ASA 162-325 mg should be given prior to PCI
- After PCI, ASA 81 mg/d should be continued indefinitely
- Loading dose of $P2Y_{12}$ Inhibitor should be given as early as possible or at time of PCI and continued for 1 year in pts who receive a stent

Pharmacologic Therapy
STEMI and Fibrinolysis: Antiplatelet

- ASA 162-325 mg and clopidogrel should be given to pts with STEMI who receive fibrinolytic therapy
- ASA 81 mg/d should be continued indefinitely and clopidogrel should be continued for at least 14 days and up to 1 yr in pts who receive fibrinolytic therapy

Pharmacologic Therapy
STEMI and PCI: Anticoagulation

- Unfractionated Heparin (UFH) prior to PCI ± GP IIb/IIIa receptor antagonists at start of PCI (if large clot burden)
- Anticoagulation can be discontinued at the end of successful PCI
- Bivalirudin monotherapy if high risk for bleeding instead of UFH & GPIIb/IIIa Inhibitors

Pharmacologic Therapy
STEMI and Fibrinolysis: Anticoagulation

- Anticoagulantion with UFH, enoxaparin, or fondaparinux prior to fibrinolysis and continue for up until discharge

Early Pharmacologic Therapy (ED)
NSTEMI/UA

- Oxygen: if O2 sats < 90%
- Nitroglycerin: SL for all pts. Follow with IV NTG in pts with HTN, ongoing discomfort, pulmonary congestion
- Aspirin: 162-325 and $P2Y_{12}$ Inhibitor (clopidogrel, prasugrel, ticagrelor) prior to PCI
- Anticoagulant (UFH, enoxaparin, fondaparinux, or bivalirudin)

Pharmacologic Therapy
NSTEMI/UA and Conservative: Antiplatelets

- ASA should be administered on presentation and continued indefinitely
- Loading dose of $P2Y_{12}$ Inhibitor should be given as early as possible and continued for up to 1 year

Pharmacologic Therapy
NSTEMI/UA and PCI: Antiplatelets

- ASA 162-325 mg should be given prior to PCI
- After PCI, ASA 81 mg/d should be continued indefinitely
- Loading dose of $P2Y_{12}$ Inhibitor should be given as early as possible or at time of PCI and continued at least 1 year in pts who receive a stent. Continuation beyond 1 yr may be considered in pts with DES

Pharmacologic Therapy
NSTEMI/UA and Conservative: Anticoagulation

- Continue heparin, enoxaparin, or fondaparinux for up until discharge

Pharmacologic Therapy
NSTEMI/UA and PCI: Anticoagulation

- Unfractionated Heparin (UFH) prior to PCI ± GP IIb/IIIa receptor antagonists at start of PCI (if large clot burden or high risk)
- Bivalirudin monotherapy if high risk for bleeding instead of UFH & GPIIb/IIIa Inhibitors
- Continue anticoagulation until the end of successful PCI

ESC Guidelines (Europe) for ACS
Differences from ACCF/AHA

- STEMI and NSTEMI/UA
  - Prasugrel or ticagrelor as first line over clopidogrel for primary PCI. Clopidogrel for fibrinolysis
  - DES preferred over BMS unless unable to comply with DAPT
- STEMI
  - Bivalirudin preferred over other anticoagulants
  - Enoxaparin preferred over heparin for anticoagulation in fibrinolysis and in PCI

Pharmacotherapy
Fibrinolytics

- Clot lysis
- First line (fibrin-specific): alteplase, reteplase, tenecteplase
- Second line: streptokinase (non-fibrin specific)
- Indicated in pts with STEMI and no access to PCI or door-to-balloon time > 90 min
- Not indicated in pts with UA/NSTEMI
- Dosed per weight and given over 1-2 hours
- Mortality benefit greatest with early administration, diminishes > 12h
- C/I in any patient with an increased risk for major bleeding
- Expensive, bleeding risk

Pharmacotherapy
Aspirin

- Additive effect to fibrinolytics, helps prevent acute occlusion during PCI
- Loading dose 162-325, then 81 mg/d indefinitely in all ACS pts

Pharmacotherapy
$P2Y_{12}$ Inhibitors

- Clopidogrel, prasugrel, ticagrelor
- Indicated for use as part of early pharmacotherapy for all ACS pts
- Dual Anti-Platelet Therapy (DAPT) with ASA
- DAPT prevents subacute stent thrombosis, death, MI, or need for repeat PCI
- Loading dose followed by maintenance
- Clopidogrel: 600 mg LD, 75 mg QD, except in fibrinolysis (300 mg ≤ 75 y/o, 75 mg > 75 y/o)

Pharmacotherapy
$P2Y_{12}$ Inhibitors

- Pro-drugs, metabolized by CYP450 to active Rx (Ticagrelor is exception)
- Drug interactions
  - Clopidogrel metabolized by CYP2C19
  - CYP2C19 inhibitors should be avoided, i.e. omeprazole, esomeprazole, fluoxetine, fluconazole, grapefruit juice, cimetidine
  - Pantoprazole has lowest inhibition amongst PPIs
  - Prasugrel less dependent on CYP450 for conversion to active Rx, so less prone to intxns

Pharmacotherapy
$P2Y_{12}$ Inhibitors

- Should be stopped 5-7d prior to any surgery
- With clopidogrel, mutation in CYP2C19 can lead to higher rate of CV events or stent thrombosis after PCI. Genetic testing advised in certain high risk pts.
- Use of ASA doses > 100mg/d lead to worse outcomes with ticagrelor than using < 100
- Ticagrelor's parent and active metabolite exert antiplatelet effect (not pro-drug)

Pharmacotherapy
$P2Y_{12}$ Inhibitors

- Prasugrel dose: 60 mg LD, 10 mg/d (≥60 kg), 5mg/d (< 60kg)
- Prasugrel has least significant drug-drug intxns
- Prasugrel and ticagrelor more potent than clopidogrel
- PLATO Study
  - (Ticagrelor + ASA) Vs. (Clopidogrel + ASA) in STEMI or NSTEMI with PCI or conservative mgmt
  - Ticagrelor more effective at reducing CV death, stroke, MI, and restenosis especially for pts with DM or pts with STEMI receiving primary PCI
  - Possible increased risk for bleeding with ticagrelor

Pharmacotherapy
Glycoprotein IIb/IIIa Receptor Antagonists

- Inhibit final common pathway for PLT aggreg.
- Reduces mortality and reinfarction
- Abciximab, eptifibatide, tirofiban
- Used only if PCI is anticipated
- Typically combined with an anticoagulant and DAPT
- IV bolus + infusion, continue until end of successful PCI
- Avoid giving with fibrinolytics and bivalirudin
- AE: immune-mediated thrombocytopenia with abciximab (5%), less commonly with tirofiban and eptifibatide (< 1%)

Pharmacotherapy
Anticoagulants

- UFH
  - First line anticoagulant for ACS
  - Prevents re-occlusion of infarct after reperfusion
  - IV bolus followed infusion, adjust dose per aPTT
  - Continued for 48 or until end of PCI
  - AE: bleeding, HIT/HAT (class assignment: look up!)
- Enoxaparin
  - IV bolus, maintenance dose SQ Q12h
  - Not well studied in primary PCI, preferred in fibrinolysis or conservative management of UA/NSTEMI
  - Continued for 8d or hospital D/C

Pharmacotherapy
Anticoagulants

- Bivalirudin
  - Direct thrombin inhibitor
  - Can be used instead of UFH for primary PCI if high bleed risk. May be safer and more effective than heparins + GP IIb/IIIa Inhibitors
  - D/C at end of PCI
- Fondaparinux
  - Factor Xa Inhibitor
  - Not recommended as a *sole* anticoagulant in PCI
  - Given SQ daily
  - Continued for 8d or hospital D/C

Pharmacotherapy
Other Agents Used in ACS

- Nitrates
  - IV NTG infusion for pts with persistent chest discomfort after 3x SL NTG, HTN, pulm congestion
  - Continue for up to 24h
  - C/I if pt received PDE-5 inhibitors w/in 24h, or tadalafil within 48h

Pharmacotherapy
Secondary Prevention following MI

- ACEIs
  - Reasonable for pts with ACS
  - Initiate in the first 24h unless C/I, continue indefinitely
- Beta-Blockers
  - Administer orally in the first 24h unless C/I, continue indefinitely

Pharmacotherapy
Secondary Prevention following MI

- Statins
  - High intensity statin (i.e. Atorva 80 mg/d or rosuva 20 mg/d) regardless of baseline lipid levels
  - Initiate as early as possible
  - Avoid use with fibrates. Rosuva safer in drug-drug intxn than atorva (CYP 3A4)
  - Monitor LFTs, myopathy