Therapies in Unstable Angina(UA)/NSTEMI
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Oxygen
- Increase supply to ischemic tissue
- Evidence from non-randomized studies
- Typically, initiate oxygen therapy via nasal cannula to maintain $O_2$ saturation greater than 90%
- Therapy is usually maintained for approximately 48 hours as arterial $PO_2$ is reduced for about this period of time in many uncomplicated acute myocardial infarctions (AMI)
- Cautioned overuse as may cause vasoconstriction and in patients with COPD

Aspirin
- Blocks the production of COX$_1$ and subsequently thromboxaneA$_2$
  - The latter is a potent mediator of platelet aggregation and vasoconstriction
- In patients with UA the US Veterans Administration Study showed a 41% risk reduction in death and MI at 12 weeks
- In patients with AMI the ISIS-2 trial showed that addition of Aspirin to streptokinase decreased mortality to 9.4% compared to 11.8% in the placebo arm;
- Recommended 162 – 325 mg to be chewed on admission, then 81 – 325 mg daily, thereafter
- Contraindicated only in true allergy, or unable to ingest oral medication (consider suppository, if necessary)

Unfractionated Heparin(UFH)
- Inactivates complexes with coagulation factors Xa, and thrombin, IXa, and Xla → by activating antithrombin III → decreased thrombus formation
- In a study by Therou et al, fatal and non-fatal MI was reduced from 7.5% to 1.2% with the use of UFH against placebo
- In the RISC study the use of ASA and UFH had a significant reduction in death and MI at 5 days
- Currently, given Heparin bolus 60-70 U/kg (max. of 5, 000U), followed by infusion of 12-15 U/kg/h (max. of 1,000U/h) and titrated for ~ PTT 50-70 seconds
- Precaution
  - Active bleeding
  - Recent intracranial, intraspinal, eye surgery
  - GI bleeding
  - Bleeding disorders
Severe hypertension

**Low Molecular Weight Heparin (LMWH)**
- Inhibits factor Xa with less plasma protein binding, thereby making the antithrombotic effects more predictable
- Stimulate platelets less and are less associated with heparin-induced thrombocytopenia
- A combined analysis of the data from ESSENCE and TIMI-11B showed a statistically significant reduction in the rate of death or MI in patients treated with LMWH
- The recent trial SYNERGY designed to compare the two heparins, showed that LMWH was as effective as UFH
- Enoxaparin 1 mg/kg S/C bid (max. of 100 mg)
- Dalteparin 120 IU/kg S/C bid (max. of 10,000 U)
- Caution should be taken in use with patients with renal insufficiency, and should NOT be used in patients with a creatinine clearance of < 30 ml/min
- If concerned about therapeutic effects can monitor Anti Xa levels and adjust dosing for levels between 0.7 – 1.0

**Thienopyridines**
- Are structurally similar to inhibitors of ADP-dependent platelet activation
- CAPRIE compared Clopidogrel and Aspirin and found a reduction in risk of vascular death, MI, stroke of 8.7% (significant)
- The CURE trial showed a statistically significant difference in primary composite outcome of CV death, nonfatal MI, or stroke of 11.4% in the Aspirin group and 9.3% in the group who received Clopidogrel and Aspirin
- Clopidogrel is given as an initial oral loading dose of 300 mg, followed by 75 mg daily
- Used for 1 month post stenting and 6 months post stenting with drug eluting stents
- In patients with ischemic event on ASA, patient may be placed on thienopyridine in addition to ASA (failed Aspirin therapy)
- Observe for thrombocytopenia

**β-Blockers**
- Decrease heart rate and improve contractility of heart muscle, thereby acting as an anti-ischemic, anti-arrhythmic, and anti-hypertensive
- Use of early IV β-Blockers in AMI in over 27, 000 (meta-analysis) patients showed a absolute risk reduction from 4.3% to 3.7% (6
lives saved/1000) –ISIS I being the largest trial included which used IV Atenolol in the first 1-2 days post AMI.
- The benefits seen were largely due to decrease in sudden death and cardiac rupture
- No studies have been done in the fibrinolytic era
- Give Metoprolol IV 5 mg q 5 min to a max. of 15 mg, and then initiate oral dosing
- Contraindicated in patients with bradycardia, prolonged PR interval, or other conduction abnormalities, evidence of acute heart failure, and inferior infarction, reactive airway disease

**Angiotensin Converting Enzyme Inhibitor (ACEI)**
- Blocks the conversion of angiotensin I to angiotensin II, with subsequent effects of NO that result in vasodilation
- Based on GISSI-3 and ISSI-4 the use of Lisinopril was shown to decrease mortality at 6 weeks (8 lives saved/1000)
- Extrapolating from the results from CONSENSUS II caution must be exercised to avoid hypotension with the use of ACEI, as there was an increase in mortality in patients with systolic blood pressures (SBP) < 90 mmHg
- Cautioned use in patients with right ventricular infarcts, bilateral renal artery stenosis, angioedema

**Calcium Channel Blockers**
- Non-dihydropyridines decrease chronotropy and inotropy of the heart and can subsequently result in hypotension; Dihydropyridines primarily affect the vascular tone and thereby have more effects on systolic blood pressure
- Dihydropyridines have been found to have no significant reduction in mortality
- The nondihydropyridine, Diltiazem, showed a 23% reduction of cardiac related death, and re-infarction in patients without evidence of heart failure
- But because of the stronger evidence for β–Blockers in the post-AMI setting, the use of the nondihydropyridines is not currently recommended as standard of therapy, but may be useful in those patients with contraindications to β–Blockers

**Nitroglycerine**
- Donation of NO to endothelium which results in vasodilation thereby improving coronary blood flow
- Has not shown to have improvement in survival based on two-large scale mortality trials involving ~ 80, 000 patients
- Given S/L as a tablet 0.3 mg or spray 0.4 mg q 5 min X 3 doses, and maybe switched to IV, if pain not completely resolved, typically at 10 mcg/min and titrated up to relief of anginal symptoms
- Continue nitrate therapy for ~ 24 hours following initial presentation
- Cautioned use in right ventricular infarcts
- Not to be used in patients who have taken Sildenafil

**Morphine**
- To reduce pain, anxiety, and oxygen demands and sympathetic tone
- Given for humane reasons and no mortality benefit has ever been studied
- Given as 2.5-5 mg IV prn