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Introduction / Classification

• "Acute MI is an event of myocardial necrosis caused by an unstable ischemic syndrome" (NEJM 2017)
• In practice, the disorder is diagnosed and assessed on the basis of clinical evaluation, the electrocardiogram (ECG), biochemical testing, invasive and noninvasive imaging, and pathological evaluation.
• All patients suspected of having an ACS should be referred to an Emergency Department with the goal of making an evaluation within 10 min (AHA/ACC guidelines).
• During initial evaluation, the clinician must determine if an ACS is present, and whether it fits one of the following clinical syndromes: (important for management)
• (taken from Anderson et al NEJM 2017)
• **Decide if STEMI or NSTEMI**, differentiation is important because:
  
  **STEMI**
  
  ▪ **= EMERGENCY!**
  ▪ Represents a complete occlusion of a coronary vessel.
  ▪ Clear mortality benefit of EARLIEST POSSIBLE reperfusion in STEMI, (<90min of chest discomfort) with thrombolytic therapy or primary PCI.
  
  **Unstable Angina or NSTEMI**
  
  ▪ Have some time to work up and treat patient
  ▪ Represents as narrowing of a coronary vessel or an unstable plaque at high risk of rupturing.
  ▪ Should undergo risk stratification if early invasive strategy (angiography) vs. medical therapy
  ▪ Often initiate medical therapy, use TIMI risk score to find risk of future CV events, symptoms, LV dysfunction, etc.. All these high risk features can drive earlier intervention.
    ▪ Use TIMI risk score to risk-stratify

• **General Pathway for ACS:**

---

**Introduction / Classification**
Physical Exam:
- Look for direct evidence of MI, as well as possible precipitants, risk factors, and consequences (i.e. HF)
- Inspection:
  - Obesity?
  - Evidence of hyperlipidemia (Xanthelasma/xanthomata)
  - Herpes Zoster
- Vital signs
- Cardiac Exam:
  - JVP
  - Heart Sounds/ Murmurs
  - Reproducible on palpation?
- Presence of PVD
  - Carotid/renal/femoral bruit
  - Peripheral pulses
  - Abdominal Aneurysm

Unstable Angina / NSTEMI

Risk Stratification
- For NSTEMI, use TIMI risk score to determine in-patient risk of CV events.
- Many TIMI trials... finally came up with:

TIMI Prognostic Variables (each = one point)

- Age ≥65 years
### TIMI Prognostic Variables (each = one point)

<table>
<thead>
<tr>
<th>Variable</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥3 Traditional CAD risk factors (HTN, DMII, Hyperlipidemia, FMhx, Smoking)</td>
</tr>
<tr>
<td>Documented CAD with ≥50% diameter stenosis</td>
</tr>
<tr>
<td>ST-segment deviation</td>
</tr>
<tr>
<td>≥2 Anginal episodes in the past 24 hours</td>
</tr>
<tr>
<td>Aspirin use in the past week</td>
</tr>
<tr>
<td>Elevated cardiac biomarkers (CK MB or troponin)</td>
</tr>
</tbody>
</table>

### TIMI Risk Score (Sum of Prognostic Variables)

<table>
<thead>
<tr>
<th>Score</th>
<th>Risk Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2</td>
<td>Low risk</td>
</tr>
<tr>
<td>3-4</td>
<td>Intermediate risk</td>
</tr>
<tr>
<td>5-7</td>
<td>High risk</td>
</tr>
</tbody>
</table>

**NOTE:**
- ASA --> highlights having active ischemia despite being on therapy.
- NOTE FOR U.S. EXAMS: GpIIAIIIB inhibitors
  - Often useful in elevated cardiac markers, and ongoing ischemia (high risk TIMI ≥5)... particularly useful in early invasive strategy.
  - Rarely used in Canada.
• In above table, the term "**Early coronary angiography**" timing is unclear.
  ◦ **TIMCS and ISAR-COWL** studies have conflicting data.
  ◦ Usually for clinically stable patients unclear when the best time to do the invasive procedure.
  ◦ No clear indication for benefit of a very rapid vs. delayed strategy (few days after presentation).

### Treatment

<table>
<thead>
<tr>
<th>Tx</th>
<th>Comments</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA-160mg PO chewed</td>
<td>Up to 21% decrease in mortality</td>
<td>Antiplatelet</td>
</tr>
<tr>
<td><strong>B-blocker</strong></td>
<td></td>
<td>B-blocker</td>
</tr>
<tr>
<td></td>
<td>Not if HR &lt;60-70 or CHF</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Careful with conduction problems on ECG</td>
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</tr>
<tr>
<td></td>
<td>If already on B-B give extra dose</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Lately: controversial, IV dose can increase incidence of cardiogenic shock in MI pts).</td>
<td></td>
</tr>
<tr>
<td><strong>Heparin</strong></td>
<td></td>
<td>Anticoag.</td>
</tr>
<tr>
<td></td>
<td>Bivalirudin can be used if history of HIT.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>For UA or NSTEMI:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Enoxaparin for 8 days or until discharged [ESSENCE trial] - preferred to UFH</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• UFH x 48hrs if not revascularized (longer if still chest pain)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>For STEMI:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• UFH or LMWH (no difference) if NOT reperfused</td>
<td></td>
</tr>
<tr>
<td>Tx</td>
<td>Comments</td>
<td>Controls</td>
</tr>
<tr>
<td>----</td>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td><strong>UFH preferred over LMWH for PCI or lytic therapy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Second Antiplatelet</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Plavix (Clopidogrel)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>(Given with ASA - dual anti-plt)</em></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| - NSTEMI: 300mg load + 75mg po daily | ▪ Proven with STEMI when added to ASA  
▪ The only issue is if you suspect triple-vessel disease, patient may need CV surgery, do not give plavix (will delay OR). | Antiplatelet |
| - STEMI: 600mg load. OR Prasugrel OR Ticagrelor | | |
| **Gp IIb/IIIa inhibitors** | If TIMI ≥5 (in NSTEMI) | Antiplatelet |
| **Nitroglycerin 0.3mg SL q5min x3** *(IF NO RV Infarct!)* | ▪ Give sublingual nitrates to all patients except pts in inferior MI and evidence of RV involvement.  
▪ Suspect RV infarct on all inferior infarcts - do 15 lead ECG to confirm (ST elevation in V4R lead) (SEE BELOW)  
▪ Mechanism: reduce preload, drops venous capacitance, improves coronary flow  
▪ If continued chest pain, start nitro drip. | Pain |
| **Morphine (1-2mg IV/SC x1)** | ▪ Suppresses heightened sympathetic response, helps beyond pain | Pain |
| **O2** *(Only if hypoxemia)* | ▪ Only if hypoxemia, but all patients end up getting it. | |

**Red – Improves survival**

**Green – Symptom Management**

**Blue - Longer Term management:**

- NOTE: No indication for antiarrhythmics (like lidocaine) to prevent ventricular arrhythmias.

**Special: RV Involvement**

- In RV infarcts, must give lots of volume to push blood through weak RV. (think of it as if it becomes a "passage chamber").
- Giving nitrates will decreases passage, LV preload, leading to hypotension and cardiogenic shock. This is called "preload dependent".
- If R-sided HF (high JVP etc) with clear lung fields, hypotension --> suspect RV infarct, give fluids
Mortality Benefit

- ASA + clopidogrel/prasugrel/ticagrelor
- B-Blocker (if heart rate and BP permit)
- Anticoagulation
  - Examples:
    - Heparins (used in low TIMI risk, but provides more benefit in medium-high risk groups).
    - Unfractionated Heparin (early invasive approach, in setting of kidney disease)
    - LMWH (Twice daily SC injection).
    - Direct Thrombin Inhibitors (Bivalirudin)
    - Used as an alternative to heparins.
    - ACUITY Trial: evaluated moderate-to-high risk unstable angina or NSTEMI treated with bivalirudin + GIIbIIIa vs. UFH+GIIbIIIa vs. bivalirudin, undergoing early invasive strategy to evaluate coronary arteries.
      - Rates of death, MI, repeat revascularization was similar, but lower risk of bleeding complications in bivalirudin monotherapy group.
  - Decision to use them based on TIMI risk, timing of cath, consideration of risk of bleed etc.
- Statins
  - Clearly has role in primary and secondary prevention.
  - Benefit of intense lipid lowering in early phase is unknown.
  - Studies (MIRACL and PROVE IT trials): high dose statin therapy soon after ACS (i.e. within 24-96hrs), reduces long-term CV events at 18mo and 2 years.
  - 80mg of atorvastatin typically regarded as "intensive therapy" with a composite benefit (mortality, CV events etc.).
  - Current consensus: High dose statin, with an LDL target of (<100mg/dL or <2.59mmol/L).
    - I.e. 40 or 80mg of atorvastatin.

Thrombolysis?

- Use of thrombolytics studied, worsens outcomes in NSTEMI.

Timing of Angiography

- Optimal timing unclear for clinically stable patients.
- TIMCS trial and ISARCOOL have conflicting information.
- No clear indication for rapid strategy vs. more delayed (i.e. few days after presentation). 8

STEMI

- Important to triage patients to early reperfusion.
- EMS do ECGs and triage patients
- As for 2014 up to 1/3 of STEMI patients don't receive reperfusion therapy!!!
- Rapid Assessment: (Many causes of CP and ECG STEMI including:)
  - Pericarditis
  - PE
  - Aortic dissection (inferior wall ST elevation) if dissection plane extends into RCA.
  - Must perform focused history (type of pain, prev CAD etc.).
    - Note: some patients (Diabetes with neuropathy, Elderly) come in with non-specific symptoms (SOB, confusion).
    - I.e. Longstanding diabetic presenting with DKA --> look for acute MI.
- Step 1 - Decide if reperfusion therapy is indicated:
  - Symptom onset <12hrs --> YES (Class I-A)
  - Symptom onset 12-24hrs --> USUALLY (Class IIa-B) - if evidence of ongoing ischemia (clinical/ecg)
  - Cardiogenic Shock, Severe HF (regardless of time from MI) --> (Class I Level B)

- Step 2 - Decide if reperfusion therapy is Thrombolysis vs. PCI
  - FMC-to-Device would be > 2hrs? (FMC = First Medical Contact)
    - If >2hrs --> Thrombolysis (perform within door-to-needle time of 30min)
    - If <2hrs --> PCI (transfer with door-in-door-out time of 30min)
Thrombolysis

- **Adjunctive therapy to support Thrombolysis**
  - ASA 162mg before thrombolysis
  - Clopidogrel 300mg before thrombolysis (75mg dose for pts ≥ 75yo) → continue for 2w to 1yr
  - Anticoagulation for at least 48hrs
    (duration: until end of hospitalization, up to 8 days, or until revascularized)
    - UFH (weight-based IV bolus + infusion, monitor aPPT 1.5-2.0 times control)
      - Continue x48hrs or until revasc
    - Enoxaparin (weight, age, CrCl dosing) IV bolus then in 15min SC injection
      - Continue for duration of hospitalization or until revasc
    - Fondaparinux initial IV dose, then in 24hrs daily SC injections (if CrCl > 30)
      - Continue for duration of hospitalization, up to 8 days, or until revasc
  - NOTE: All Class I indications evidence level B, but enox has level A.

- **Steps After thrombolysis:**
  - Did Thrombolitics Work?
Successful Reperfusion Indicators:

1. Resolution of Chest Pain
2. >70% ST-segment resolution on ECG (some say 50%)
3. Reperfusion arrhythmias (such as AIVR)

If reperfused:

- Risk stratify the patient based on risk of future CV events.
- **Arrange transfer to PCI center**
  - Poor prognostic features requiring PCI transfer (based on old guidelines):
    - Cardiogenic Shock
    - Severe HF
    - Failed Reperfusion
    - Or other high-risk features (i.e., low EF, hypotension, HF, shock)
    - (B/c concern large patient myocardium at risk, patient won’t tolerate future MI)

If NOT reperfused

- Urgent transfer to PCI-capable center for "rescue PCI"

**Transfer to PCI Center**:

- NEW Evidence: Transfer to PCI center whether or not they reperfused, regardless if they have hemodynamic instability etc..
  - **NEJM 2009 TRANSFER-AMI Trial** --> RCT comparing delayed angiography vs. early coronary angiography post-thrombolysis: early angiography = lower risk of reinfarction and recurrent ischemia (no diff in mortality)

**Fibrinolytic Therapy (Circulation 2004;110:588)**

**Absolute Contraindications**

- Any prior ICH
- Known structural cerebral vascular lesion (ie. AVM)
- Known malignant intracranial neoplasm
- Ischemic stroke within 3mo (except acute ischemic stroke within 3h)
- Suspected aortic dissection
- Active bleeding (excluding menses)
- Significant closed head/face trauma in last 3mo

**Relative Contraindications**

- History of chronic/severe/poorly controlled HTN
- Severe uncontrolled HTN at presentation (SBP > 180 mmHg, or dBP > 110 mmHg)
- History of ischemic stroke >3mo or known other intracranial pathology
- Traumatic prolonged (>10min) CPR, or Major Surgery within <3 weeks
- Recent (<4w) internal bleeding
- Non-Compressible vascular puncture
- Pregnancy
- Active peptic Ulcer
- Current use of anticoagulants (the higher INR, the greater bleeding risk)

**Primary PCI**

- **Adjunctive therapy to support Primary PCI**
  - ASA 162mg given before PCI (continue indefinitely post-PCI)
• P2Y12 receptor inhibitor (continue x1 year regardless of BMS/DES stent)
  ▪ Clopidogrel 600mg → continue 75mg daily x1 year
  ▪ Prasugrel 60mg → continue 10mg daily x1yr (contraind. if prior stroke/TIA)
  ▪ Ticagrelor 180mg → continue 90mg bid x1yr
• Consider IV GP IIb/IIIa (large thrombus burden, inadequate P2Y12 loading)
  ▪ inhibitors before PCI (+/- stent, +/- clopidogrel) who are receiving UFH.
  ▪ Not used with bivalirudin
    ▪ Abciximab, high-bolus-dose tirofiban, or double-bolus ptifibatide
    ▪ Can give them in ED, EMS, cath lab (only if the decision to do PCI is made!!!)
    ▪ intracoronary abciximab can be used
    ▪ Can continue GP IIb/IIIa beyond 1yr in pts with DES
• Anticoagulation (consider in case-by-case basis)
  ▪ Options:
    ▪ UFH (with boluses to keep aPTT therapeutic) [be careful if GP IIb/IIIa is used]
    ▪ Bivalirudin (with or without prior tx with UFH)
  ▪ If bleeding risk is HIGH, use bivalirudin monotherapy instead of UFH+GP IIb/IIIa
  ▪ NOTE: Do not use fondaparinux (catheter thrombosis risk)

• Angiography in STEMI NOTES:
  ▪ PCI should NOT be performed in non-infarct artery at the time of primary PCI in hemodynamically stable STEMI patients (Class III-B) → EVIDENCE OF HARM. (conflicting studies) [Unless cardiogenic shock]
  ▪ "No Reflow" Phenomenon → occurs when poor perfusion despite restoration of epicardial flow
    ▪ Thought to be due to inflammation, endothelial injury, edema, atheroembolization, vasospasm, reperfusion injury
    ▪ Associated with poor survival rate
    ▪ Possible treatment/prevention: (all have inconsistent effect)
      ▪ Use of GP IIb/IIIa antagonist (abciximab)
      ▪ Vasodilators (nitroprusside, verapamil, adenosine)
      ▪ Metabolism Inhibitors (nicorandil, pexelizumab)
      ▪ Manual thrombus aspiration (positive studies, but not all showed positive results)
  ▪ Manual aspiration thrombectomy is reasonable undergoing primary PCI (4 studies - Class IIa-B)
  ▪ Do not PCI of CTO (total occlusion) infarct artery >24hrs after STEMI (Class III Level B)
    ▪ If stable, no severe ischemia, and 1 or 2-vessel disease
    ▪ OAT Trial (Occluded Artery Trial) - higher re-infarction rates if try to open a CTO >24hrs occluded.
  ▪ Non-Infarct Artery PCI: (AFTER primary PCI)
    ▪ DO NOT open at time of primary PCI.
    ▪ Only if spontaneous symptoms of ischemia (Class I, Level C)
    ▪ Intermediate or high-risk findings on non-invasive testing (Class IIA, Level B)

• Other Notes:

• Blood sugar control
  ▪ Study: Intense glucose control (4.5-6mmol/L) ass’d with increased mortality!!! (hypoglycemica) This is a new guideline: glucose <10mmol/L. (ICU patients, but included ACS)
  ▪ Study: ACS patients with high glucose = worse outcomes.
  ▪ DIGAMI: mortality at 1 year, 28% RRR, and 11% absolute if randomized to aggressive glucose control. (not acute ICU, but for recovery).
• Hence, this is a long-term outcome measure, acutely can be lenient (<10) but chronically in recovery should be more strict.

• Balloon pumps
  • If cardiogenic shock, or decreased LV function, can put in balloon pump.

Other STEMI Syndromes
  • Other disease can give same syndrome:
    • Vasospastic Prinzmetal Angina (uncommon) - Classically at rest associated with transient ST segment elevation/depression, occurs in normal or near-normal coronary artery segments.
      ▪ Treated with vasodilator therapy long-term such as CCB or long-acting nitrates.
      ▪ Provoked by use of illicit drugs (cocaine, methamphetamine).
      ▪ Presence of the plaque in coronary artery is a strong precipitant of vasospasm at the same site.
    • Takotsubo
      ▪ Japanese octopus trap that shaped like LV when have apical ballooning.
      ▪ Aka Stress-Induced Cardiomyopathy - significant impairment of LV contractility in typical pattern (distal anterior wall, apex, distal inferior wall) with preserved function in basal segments of the heart.
      ▪ No obstructive coronary lesions usually present with mild elevation of enzymes, but not to the degree that affects so much of the LV.
      ▪ Supportive care → Almost always reversible.

Thrombolytics
  • If time to PCI > 120min, and no contraindications, can give thrombolytic therapy:
    • Within 12 hours (Class I, Level A)
    • Within 12-24 hours (Class IIa, Level C) - if ongoing ischemia (ecg or clinical) and large area of myocardium at risk (or hemodynamic instability)
  • DO NOT give fibrinolytics to ST depressions
    • Unless posterior (inferobasal) MI suspected, (or associated STE in aVR)

• Adjunctive Therapy
  • All thrombolized patients should receive:
    ▪ ASA (162mg) + 80mg daily indefinitely AND
    ▪ Clopidogrel (300mg if ≤ 75yo and 75mg if >75yo) + 75mg daily for at least 14 days (level A) to 1yr. (Level C)
    ▪ Anticoagulation at least >48hrs up to 8 days (or until revascularized)
      ▪ UFH (wt-adjusted IV bolus+infusion to aPTT 1.5-2.0x control) x48hrs or revasc
      ▪ Enoxaparin (age, wt, CrCl) IV bolus + in 15min by SC injection up to 8 days or until revasc.
      ▪ Fondaparinux (if CrCl > 30mL/min) IV dose, followed in 24hrs by daily SC up to 8 days or until revasc.
      ▪ (helps vessel patency, prevents reocclusion)
  • Post-Thrombolysis Transfer
    • Immediate transfer to PCI center for angiography if: (SHOCK Trial - STEMI+shock --> revasc improves mort)
      ▪ Acute Severe HF
      ▪ Cardiogenic Shock (Class I Level B)
    • Urgent transfer to PCI center for angiography if:
      ▪ Evidence of failed reperfusion (or reocclusion) (Class IIA, Level B)
    • Routine Transfer for "routine early coronary angiography" (even if stable, and successful reperfusion)
      ▪ For Angiography within 24hrs (but not within 2-3hrs post-lytics - to monitor for bleeding) (Grade IIa, Level B)
      ▪ TRANSFER-AMI Trial (less recurrence ischemia/infarction)
• Post-Thrombolysis PCI
  ◦ ASA indefinitely
  ◦ Clopidogrel
    ▪ 300mg load (if no prev load, and within 24hrs of lysis)
    ▪ 600mg load (if no prev load, and >24hrs of lysis)
    ▪ (Followed by 75mg daily)
  ◦ Prasugrel
    ▪ 60mg load (once coronary anatomy is known, and no prev plavix load)
    ▪ DO NOT give within 24hrs of fibrin-specific agent
    ▪ DO NOT give within 48hrs of non-fibrin-specific agent.
    ▪ Follow by 10mg load.
    ▪ DO NOT give if prior stroke/TIA

• In absence of contraindications, can give thrombolytic therapy to pts with STEMI and onset of symptoms in previous 12hrs.
  (When antidipated time to PCI > 120min)
• Patient receiving fibrin-specific fibrinolytics --> also give UFHeparin (prevent re-occlusion of infarct artery). Half-life of fibrinolytics is short (LMWH can also be used)
• Agents available:

### Characteristics of Thrombolytic Agents Used in the Treatment of STEMI (RED: more common)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Streptokinase (SK)</th>
<th>Alteplase (tPA)</th>
<th>Reteplase (rPA)</th>
<th>Tenecteplase (TNK)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose</td>
<td>1.5 million units over 30-60 min</td>
<td>15mg IV bolus, +0.75 mg/kg over 30m +0.5 mg/kg over 60m (Total = 90m)</td>
<td>10 units × 2 (30 min apart) each over 2 min</td>
<td>30-50 mg (wt based)</td>
</tr>
<tr>
<td></td>
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<td>10 units × 2 (30 min apart) each over 2 min</td>
<td>30-50 mg (wt based)</td>
</tr>
<tr>
<td>Bolus administration</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*Based on body weight.

*TIMI flow grade 2/3 refers to mildly impaired flow through the coronary artery involved in the myocardial infarction. The higher the percentage of TIMI 2/3 flow, the more effective the thrombolytic agent.


Urokinase = used only for PE. T
<table>
<thead>
<tr>
<th>Characteristic</th>
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<th>Reteplase (rPA)</th>
<th>Tenecteplase (TNK)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergic reaction possible on repeat exposure</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>TIMI flow grade 2/3b</td>
<td>~55%</td>
<td>~75%</td>
<td>~83%</td>
<td>~83%</td>
</tr>
<tr>
<td>Rate of intracerebral hemorrhage</td>
<td>~0.4%</td>
<td>~0.4-0.7%</td>
<td>~0.8%</td>
<td>~0.9%</td>
</tr>
<tr>
<td>Fibrin specificity (theoretically reduce bleeding)</td>
<td>None</td>
<td>+++</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Mechanism (all convert plasminogen to plasmin --→ break down fibrin)</td>
<td>Acts on circulating fibrinogen (systemic lytic state)</td>
<td>Acts on fibrin-bound plasminogen (more specific)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Notes:</td>
<td>- bacterial protein - Produces fever in 20–40%, can get neutralizing antibody. <strong>No longer used</strong></td>
<td>- More common - Survival benefit over SK - <strong>Newer agents act faster, infuse faster.</strong></td>
<td>- Variant of tPA (alteplase) - Developed for more rapid clot lysis (but in trials does not have better outcomes than tPA</td>
<td>- faster clot lysis time but mortality rate same as other agents</td>
</tr>
</tbody>
</table>

| Any of above can be used (except Streptokinase), but rPA and TNK preferred due to bolus dosing and faster clot lysis (even though has no mortality benefit) |

*Based on body weight.

**TIMI flow grade 2/3** refers to mildly impaired flow through the coronary artery involved in the myocardial infarction. The higher the percentage of TIMI 2/3 flow, the more effective the thrombolytic agent.


Urokinase = used only for PE. T
• **Adverse effects:**
  - | **Complication**                  | **Rate**               |
  - | Intracranial Hemorrhage (most feared) | 0.5 - 1.0 % (risk same with tPA, rPA, and TNK) |
  - | Bleed requiring transfusion            | 5-15%               |

• **Thrombolytic reversal:** Replete fibrinogen levels with cryoprecipitate (10-15 bags needed) to raise fibrinogen level to 1 g/L
  - Can also infuse FFP up to 6 units for additional fibrinogen and volume!
  - Antifibrinolytic agents such as epsilon-aminocaproic acid (5g over 15-30m IV), discouraged due to widespread thrombosis.

Contraindications to Thrombolytic Therapy for ST-Elevation Myocardial Infarction

<table>
<thead>
<tr>
<th>Absolute Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any previous intracerebral hemorrhage</td>
</tr>
<tr>
<td>Known cerebrovascular lesion (e.g., arteriovenous malformation)</td>
</tr>
<tr>
<td>Ischemic stroke within 3 months</td>
</tr>
<tr>
<td>Suspected aortic dissection</td>
</tr>
<tr>
<td>Active bleeding or bleeding diathesis (excluding menses)</td>
</tr>
<tr>
<td>Significant closed head or facial trauma within 3 months</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Relative Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of chronic, severe, poorly controlled hypertension</td>
</tr>
<tr>
<td>Severe uncontrolled hypertension on presentation (SBP &gt;180 mm Hg or DBP &gt;110 mm Hg)</td>
</tr>
</tbody>
</table>
  (OK if can lower to <140/90)                                                            |
| History of ischemic stroke (>3 months), dementia, or known intracranial pathology       |
| Traumatic or prolonged (>10 minutes) CPR or major surgery (<3 weeks)                    |
| Recent (within 2-4 weeks) internal bleeding                                              |
**Absolute Contraindications**

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Noncompressible vascular puncture site</td>
</tr>
<tr>
<td>For streptokinase/anistreplase: previous exposure (&gt;5 days) or previous allergic reaction to these agents</td>
</tr>
<tr>
<td>Pregnancy</td>
</tr>
<tr>
<td>Active peptic ulcer disease</td>
</tr>
<tr>
<td>Current use of anticoagulants: the higher the INR, the higher the bleeding risk</td>
</tr>
</tbody>
</table>

- NOTE: If has relative contraindications, usually PCI transfer is preferred to lytics.
- "Facilitated PCI" - Sometimes have pre-treatment lytics followed by PCI, but recent studies indicated increased adverse events (bleeding).

**CABG for STEMI**

- Urgent CABG for STEMI and coronary anatomy not amenable to PCI:
  - IF ongoing or recurrent ischemia, shock, severe HF, or other high risk features (Class I, Level B)
  - IF no shock, not candidates for PCI or lytic therapy --> CABG within 6hrs (Class IIb, Level C)
- CABG is recommended in pts with STEMI if repairing mechanical defects. (Class I, Level B)
- Use of mechanical support is reasonable for STEMI, hemodynamically unstable, and need urgent CABG.

**Managing Antiplatelets around CABG**

- ASA should not be withheld before urgent CABG (Class I, Level C)
- Clopidogrel or ticagrelor should be d/c at least 24hrs before urgent on-pump CABG if possible (Class I, Level B)
- IV GP IIb/IIIa
  - Eptifibatide, tirofiban d/c 2-4hrs before urgent CABG (Class I)
  - Abciximab at least 12hrs before urgent CABG (Class I)
- Urgent off-pump CABG within 24hrs of plavix/ticagrelor can be considered (Class IIb, Level B)
  - (esp if benefits of revasc outweigh risks of bleeding)
- Urgent CABG within 5 days of clopidogrel or ticagrelor (or 7 days after prasugrel) can be considered (Class IIb, Level C) [benefits vs. risks]
- **Summary: Plavix+Ticagrelor d/c 24hrs before urgent CABG (Class I) or 5 days before CABG (Class IIb)**
  - Prasugrel = 7 days.

**Post-STEMI**

- B-Blocker within 24hrs (Class I)
  - Continue during and after hospitalization
    - Contra-indications:
      - HF
      - Low output state
      - High risk of cardogenic shock
      - Other (AV block >240ms, asthma, 2nd or 3rd deg AVB)
        - If contra-indicated, re-evaluate later.
      - Acutely: Can consider IV BB if ongoing ischemia (Class IIa, Level B)
    - ACEi within 24hrs:
      - Class I, Level B -> Anterior STEMI, HF, LVEF < 40%
Class IIa, Level A --> TO ALL PATIENTS WITH STEMI

- ARB if intolerant to ACE.
- Aldosterone antagonist with BB and ACEi if EF < 40% AND:
  - Symptomatic HF
  - DMII

Complications

Status: Under Construction: PENDING REVIEW

- Look for shock, new murmurs, HF, which often occur several days post-MI when necrosis happens
- **LV systolic dysfunction**
  - Heart failure --> reduce preload (for symptoms), afterload reduction w/ ACEi to reduce work load and adverse LV remodeling.
  - **Cardiogenic shock**
    - Very high risk of death!
    - Very common with RV infarct, which requires fluid resuscitation (no preload reduction!)
- **Note on RV Infarcts:**
  - **Clinical Features of RV Infarct**
    - Hypotension
    - Clear lung fields
    - Elevated JVP
  - Get a RIGHT-sided ECG (V3R and V4R leads -> look for >1mm ST Elevation)
- **Treatment:**
  - Give FLUIDS to fill the RV, give dopamine or dobutamine if hypotension persists.
  - Can take up to 3 days for RV to recover, even if revascularized.
- **Mechanical complications**
  - **VSD** (ischemic/necrotic myocardium)
    - Anterior or Inferior MI (transmural affecting septum).
    - Often requires VSD closure, with very high surgical/medical mortality (50%).
    - Difficult due to necrotic tissue around the defect.
  - **Papillary muscle rupture** (i.e. severe acute MR)
    - Several days after MI
    - Present with acute pulmonary edema & loud systolic murmur with no thrill (pressure equilibrates rapidly) --> shock.
    - Get echo! (differentiates between VSD and papillary rupture - both loud systolic murmurs).
      - Often balloon pump is advised.
      - Nitroprusside to reduce afterload, diuretics.
      - Emergency surgery required!
    - NOTE: MR common post-MI (wall motion affecting leaflet coaptation), especially inferior wall.
  - **LV free wall rupture**
    - High mortality, often catastrophic (Pericardial tamponade & death)
    - High Risk Features:
      - Females, first MI, elderly, anterior location.
    - Symptoms:
      - Sudden feeling un well, nauseated, restless.
    - Echo findings
      - If recognize early, can salvage (pericardiocentesis, surgery).
      - Can get LV pseudoaneurism, which is a rupture contained by pericardium
        - Often requires surgery
- **Pericarditis**
  - Dressler syndrome, pericarditis 1mo post-mi.
  - OR acute pericarditis with transmural infarct.
- **Aneurism**
  - Anterior or rarely inferior infarct.
  - 3 complications:
    - Refractory HF, Clot, VT arrhythmia
    - DOES NOT RUPTURE, has all 3 layers.
    - CLOT:
      - Anticoagulation of warfarin for 3-6mo (high risk embolism).
      - 10-20% of pts with anterior STEMI will have LV thrombus.
      - Anterior wall MI used to get anticoagulation (not advised anymore). Nowadays risk is low with dual antiplatelet therapy.
- **Pseudoaneurism**
  - Very narrow neck, and very thin.
  - Can occur anywhere.
  - Higher risk of rupture

**NOTE: Bezold-Jarisch Reflex:**

Mechanoreceptor reflex triggered by mechanoreceptors in LV, trigger response of sinus bradycardia + hypotension.

- Successful reperfusion triggers this reflex to increase contractility, but results in bradycardia and hypotension.
- IV nitrates can cause this as well.
- **Treatment:**
  - IV fluids
  - Turn off IV nitroglycerin
  - Use dopamine as a temporizing measure (maintain BP until response resolves).
  - Can use atropine if bradycardia persists.

- **Arrhythmias:**
  - Transient complete heart block with anterior or inferior wall MI. (usually transient).
  - **Inferior MI + 3deg AV block**
    - Usually transient - may require temporary transvenous pacing.
- Theory: inferior wall sits on diaphragm (close proximity to vegas nerve) causing complete heart block.
  - **Anterior MI + 3deg AV block**
    - Poor prognostic sign!!
    - Permanent pacer usually needed.
    - Theory: LAD blocked, infarct proximal to HIS bundle.
  
  - **Ventricular Tachycardia**
    - **Early:** (within 24hrs)
      - Usually self-limited, may not be prognostically significant.
      - Monomorphic
        - Scar/Ischemia
      - Polymorphic
        - 1. Eletrolytes
        - 2. Ischemia
          - Use lidocaine- good for acidic environment
          - Repeat Angiography?
          - Beta-blocker (raises threshold)
    - **Late:**
      - More concerning
  
  - **Ventricular Fibrillation**
    - Often VT degenerates into VF.
  
  - **AIVR**
    - Patients with successful reperfusion can develop a wide-complex rhythm.
    - ECG shows a regular wide complex rhythm at 92/min with no clearly discernible atrial activity
    - AIVR is postulated to result from abnormal automaticity in the subendocardial Purkinje fibers.
      - Observed in up to 15% of patients who undergo reperfusion.
      - HR almost always < 120/min and can be < 100/min.
    - Most studies have shown that it is a benign rhythm when it occurs within 24 hours of reperfusion.
    - **Management:**
      - No intervention! (usually a good sign)
      - Consider Beta-Blocker if not already on one.
      - Possible to give atropine for SA node to overtake, but usually not necessary.
  
- **Atrial Fibrillation**
  - Poor prognostic sign.
  - May be caused by acutely increased left atrial pressure

### Notes on Diabetes

- Pts with diabetes: AHA recommends exercise stress testing for asymptomatic DM patients undergoing an exercise program. (No need for exercise stress testing for other pts who are asymptomatic).
- CAD and diabetes: Diabtes with triple vessel diseases need less repeat revascularization with CABG when compared to PCI.
  - Many diabetic patients with **triple vessel disease** and **LV systolic dysfunction** are advised to undergo CABG rather than PCI.
  - If PCI is pursued, most will favour DES stents because BMS have a higher rate of in-stent stenosis in DMII patients.

### Notes on Women

- **WISE study**
  - Finding normal coronaries on angio in female patient that has had an abnormal stress test -- still risk.
  - This study compared 540 women with suspected ischemia but no angiographic evidence of obstructive CAD with 1000 age- and race-matched asymptomatic cohorts. The 5-year annualized event rate for cardiovascular events was 16% in women with nonobstructive CAD (stenosis in any coronary artery of 1%-49%), 7.9% in those with normal coronary vessels (no stenosis in any coronary artery), and 2.4% in the asymptomatic cohort (P < 0.002).
  - **Exercise testing in women has lower sensitivity and specificity than men. (although recommendations are the same)**
  - Women with positive stress tests and normal coronaries can show microvascular and endothelial disfunction.
  - Reynold's Risk Score sometimes used as an alternative to Framingham's Risk Score
    - Includes additional risk factors (family hx, and hsCRP).
    - 40% of women in intermediate risk group reclassified with Reynold's Risk Score.
Postmenopausal: no benefit of estrogen therapy to reduce CV risk, and no known harm. There is a signal for breast cancer.

Women with ACS are more likely than men to have atypical anginal symptoms (fatigue, dyspnea, nausea).

Other Important Concepts

Cardiac Enzymes

- Cardiac Enzyme Types:
  - Myoglobin (old, poor area under curve)
  - CK-MB (MB isoenzyme of Creatine Kinase) - previously gold standard, but 2003 Heart study removed it
  - Troponin I (cTnI) (more sensitive and specific than CK-MB)
  - Troponin T (cTnT)
- Troponin may not be detectable until 2hrs post-onset of chest pain. (may not be detectable for up to 12h)
- Some hospitals do the new high-sensitivity troponin (something like that) hsTrp, which goes up earlier?

Reading:
- MERIT Study: Collinson PO et al (2002) Heart (compared biomarkers)
Differential for Troponin Elevation

• Myocardial Infarct
  ◦ Rise and/or fall of cardiac biomarkers (trop) with evidence of ischemia (one of):
    1. Ischemic symptoms
    2. ECG: new ischemic changes or new pathologic Q-waves
    3. Imaging: loss of viable myocardium (MIBI) or wall motion abnormality (Echocardiography).

• Type II:
  ◦ Ischemia due to increase oxygen demand or decreased vascular supply.
    • Increased demand:
      ▪ Arrhythmias, Sepsis
    • Decreased supply:
      ▪ Coronary Spasm, Coronary embolism, anemia, arrhythmias, hypertension/hypotension.