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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 10min (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:**
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>≥3 Traditional CAD risk factors (HTN, DMII, Hyperlipidemia, FMhx, Smoking)</th>
</tr>
</thead>
<tbody>
<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)**

| 0-2 Low risk |
| 3-4 Intermediate risk |
| 5-7 High risk |

- 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**
- Treat all patients with:

<table>
<thead>
<tr>
<th>Tx</th>
<th>Comments</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA-160mg PO chewed</td>
<td><strong>Up to 21% decrease in mortality</strong></td>
<td>Antplatelet</td>
</tr>
<tr>
<td><strong>B-blocker</strong></td>
<td><strong>Not if HR &lt;60-70 or CHF</strong></td>
<td>B-blocker</td>
</tr>
<tr>
<td>- Usually metoprolol PO 25mg BID</td>
<td><strong>Careful with conduction problems on ECG</strong></td>
<td></td>
</tr>
<tr>
<td>- In past used IV as well (not anymore)</td>
<td><strong>If already on B-B give extra dose</strong></td>
<td></td>
</tr>
<tr>
<td>- (Lately: controversial, IV dose can increase incidence of cardiogenic shock in MI pts).</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Heparin</strong></td>
<td><strong>Bivalirudin can be used if history of HIT.</strong></td>
<td>Anticoag.</td>
</tr>
<tr>
<td>- UFH if &gt;75, obese or sig renal failure</td>
<td><strong>Enoxaparin for 8 days or until discharged [ESSENCE trial] - preferred to UFH</strong></td>
<td></td>
</tr>
<tr>
<td>- LMWH otherwise</td>
<td><strong>UFH x 48hrs if not revascularized (longer if still chest pain)</strong></td>
<td></td>
</tr>
<tr>
<td>- Fondaparinux also an option</td>
<td><strong>For STEMI:</strong></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></td>
<td>• UFH preferred over LMWH for PCI or lytic therapy</td>
<td></td>
</tr>
<tr>
<td><strong>Second Antiplatelet</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plavix (Clopidogrel)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>(Given with ASA - dual anti-plt)</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- NSTEMI: 300mg load + 75mg po daily</td>
<td>◦ Proven with STEMI when added to ASA</td>
<td>Antiplatelet</td>
</tr>
<tr>
<td>- STEMI: 600mg load. OR Prasugrel OR Ticagrelor</td>
<td>◦ The only issue is if you suspect triple-vessel disease, patient may need CV surgery, do not give plavix (will delay OR).</td>
<td></td>
</tr>
<tr>
<td><strong>Gp IIb/IIIa inhibitors</strong></td>
<td></td>
<td>Antiplatelet</td>
</tr>
<tr>
<td></td>
<td>If TIMI ≥5 (in NSTEMI)</td>
<td></td>
</tr>
<tr>
<td><strong>Nitroglycerin 0.3mg SL q5min x3</strong></td>
<td>◦ Give sublingual nitrates to all patients except pts in inferior MI and evidence of RV involvement.</td>
<td>Pain</td>
</tr>
<tr>
<td><em>(IF NO RV Infarct!)</em></td>
<td>◦ Suspect RV infarct on all inferior infarcts - do 15 lead ECG to confirm (ST elevation in V4R lead) (SEE BELOW)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>◦ Mechanism: reduce preload, drops venous capacitance, improves coronary flow</td>
<td></td>
</tr>
<tr>
<td></td>
<td>◦ If continued chest pain, start nitro drip.</td>
<td></td>
</tr>
<tr>
<td><strong>Morphine(1-2mg IV/SC x1)</strong></td>
<td>◦ Suppresses heightened sympathetic response, helps beyond pain</td>
<td>Pain</td>
</tr>
<tr>
<td><strong>O2</strong></td>
<td>◦ Only if hypoxemia, but all patients end up getting it.</td>
<td></td>
</tr>
</tbody>
</table>

**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

• 1. ASA + clopidogrel/prasugrel/ticagrelor
• 2. B-Blocker (if heart rate and BP permit)
• 3. 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).
    OR
    ▪ 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 thrombolitics 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).

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 petic 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’ed 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 thrombolyzed 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.

### 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 antedipated 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) Halflife 5min</td>
<td>10 units x 2 (30 min apart) each over 2 min</td>
<td>30-50 mg (wt based) 60kg = 30mg 60-69kg = 35mg 70-79kg = 40mg 80-89kg = 45mg ≥ 90kg = 50mg</td>
</tr>
<tr>
<td>Bolus administration</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*aBased on body weight.

bTIMI 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>
<th>Streptokinase (SK)</th>
<th>Alteplase (tPA)</th>
<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 2/3(^b)</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 --&gt; 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.</td>
<td>- More common - Survival benefit over SK - Newer agents act faster, infuse faster.</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)

\(^a\)Based on body weight.

\(^b\)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:

<table>
<thead>
<tr>
<th>Complication</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracranial Hemorrhage (most feared)</td>
<td>0.5 - 1.0 % (risk same with tPA, rPA, and TNK)</td>
</tr>
<tr>
<td>Bleed requiring transfusion</td>
<td>5-15%</td>
</tr>
</tbody>
</table>

• **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

---

**Absolute Contraindications**

Any previous intracerebral hemorrhage

Known cerebrovascular lesion (e.g., arteriovenous malformation)

Ischemic stroke within 3 months

Susp ected aortic dissection

Active bleeding or bleeding diathesis (excluding menses)

Significant closed head or facial trauma within 3 months

**Relative Contraindications**

History of chronic, severe, poorly controlled hypertension

Severe uncontrolled hypertension on presentation (SBP >180 mm Hg or DBP >110 mm Hg)

(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

- Noncompressible vascular puncture site
- For streptokinase/anistreplase: previous exposure (>5 days) or previous allergic reaction to these agents
- Pregnancy
- Active peptic ulcer disease
- Current use of anticoagulants: the higher the INR, the higher the bleeding risk

• 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)

### Post-STEMI

- B-Blocker within 24hrs (Class I)
  - Continue during and after hospitalization
    - Contra-indications:
      - HF
      - Low output state
      - High risk of cardiogenic 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:

<table>
<thead>
<tr>
<th>Clinical Features of RV Infarct</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension</td>
</tr>
<tr>
<td>Clear lung fields</td>
</tr>
<tr>
<td>Elevated JVP</td>
</tr>
</tbody>
</table>

  ▪ 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 unwell, 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

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**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 pacemaker 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. Electrolytes
        ▪ 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: Diabetes 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 dysfunction.
  - 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.