Acute Coronary Syndromes

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ACUTE CORONARY SYNDROMES

I. INTRODUCTION

A. Epidemiology

1. 5 million annual ED visits for CP
   a. 15% AMI
   b. 25-30% UA
2. IHD leading cause of death in US
   a. 500,000 annual deaths
   b. MI still 35% mortality
3. Released MI = malpractice payouts

B. History

1. Early 1900s: advent of arrhythmia control
2. Revolution in the ’60s
   a. Catheterization
   b. CPR
   c. CCU
   d. EMS
3. Active reperfusion begun in 1980s

C. Definitions

1. All definitions necessarily retrospective
2. Stable angina
   a. Chest pain (or ischemic angina variant)
   b. Transient
   c. Episodic
   d. Reproducible
   e. Extinguishable
   f. Unchanged from previous
   g. Canadian Cardiovascular Society
      i. Class I Strenuous activity
      ii. Class II Slight limitation
      iii. Class III Severe limitation (1 block/flight)
      iv. Class IV Any activity/pain at rest
3. ACS
   a. Unstable angina: any change from previous
      i. New onset angina
      ii. Any change in provocation
      iii. Increased duration
      iv. Increased severity
v. Resistance to previous treatment
vi. Synonyms
   • Preinfarction angina
   • Accelerating angina
   • Crescendo angina
   • Intermediate coronary syndrome
   • Preocclusive syndrome
v. Evolution
   • 40% progress to AMI
   • 17% mortality without diagnosis
b. Variant angina
   i. AKA Prinzmetal’s Angina
   ii. Nonocclusive coronary vasospasm
   iii. STE with clinical features of AMI
c. Acute MI (WHO definition from 1960s): two of three
   i. Chest pain > 15-20 mins
   ii. No relief with NTG or rest
   iii. EKG changes +/- enzyme bump
d. Acute MI (2000 ACC definition) = troponin elevation plus
   one of the following:
   i. Ischemic symptoms
   ii. Q waves
   iii. ST deviation
   iv. PCI

II. PATHOPHYSIOLOGY

A. Mechanism: Tissue ischemia

   1. Lack of oxygen delivery to tissue/muscle
   2. Usually secondary to lack of blood flow
   3. Continuum of hypoxia to cell death
   4. Occlusion of coronary arteries
   5. Usually by thrombus

B. Anatomy

   1. Coronary vasculature review
      a. Left
         i. LAD
         ii. Circumflex
      b. Right
   2. Two types of thrombi
      a. White
         i. Platelet rich
         ii. Gradual onset
iii. Only partially occlusive
iv. Like rings of tree
v. Thought to be cause of UA/NSTEMI

b. Red
i. Caused by plaque rupture
   • Change in intraluminal pressure
   • Mechanical shearing forces
   • Size/thickness of fibrous cap
   • Lipid content
   • Statins: possible plaque stabilizer?
ii. Clotting factors involved
iii. Not more likely with larger lesions
iv. Causes complete occlusion
v. Sudden
vi. Thought to be responsible for STEMI

C. Tissue Damage

1. Three steps of damage
   a. Acute ischemia
   b. Vasospasm
   c. Reperfusion injury
2. Two main complications
   a. Dysrhythmias
   b. Pump failure
      i. No CHF  5% mortality
      ii. Mild CHF  15-20% mortality
      iii. Pulm edema  40% mortality
      iv. Cardiogenic shock  80% mortality
   c. Rarer: papillary muscle/valvular rupture

III. DIAGNOSIS

A. History

1. Risk factors
   a. Age / sex
   b. Traditional coronary risk factors
      i. HTN
      ii. DM
      iii. HL
      iv. Smoking
      v. FMH
      vi. Obesity
   c. Known CAD
2. Pain Quality
a. **Angina ≠ ‘Chest Pain’**
   i. Choking / Strangulation / Constriction
   ii. **Pressure**
   iii. Squeezing
   iv. Fullness
   v. Burning
   vi. Heaviness
b. If described as ‘pain’
   i. **Dull / Aching**
   ii. Less likely sharp / stabbing
c. **Location**
   i. Sternal
   ii. Left chest
d. **Radiation**
   i. Shoulder
   ii. Neck
   iii. Mandible
   iv. Arm
e. **‘Atypical’ isn’t so atypical**
   i. Above are suggestive; 24% of patients presenting this way have MI; 30% have UA
   ii. However, of all presenting with sharp / stabbing chest pain, 5% have MI / 17% have UA
   iii. Up to 20% ACS for “burning” type pain
   iv. 19% MI’s describe as stabbing
f. **Duration guidelines**
   i. Angina < 15 min
   ii. MI > 15 min
   iii. Generally not ACS when < 1 second
   iv. Hours of pain = large differential
g. **Provocation**
   i. Exertion
   ii. Cold
   iii. Food
h. **Relief**
   i. Rest
   ii. NTG
   iii. (reperfusion)
i. **Associated symptoms**
   i. Diaphoresis
   ii. N/V
   iii. Dizziness
   iv. Anxiety
   v. Dyspnea
j. **Anginal Equivalents**
   i. **Dyspnea (30% AMIs!)**
ii. Radiation pain alone
iii. Dizziness
iv. Weakness
v. Diaphoresis

3. Special populations
   a. Elderly
      i. Pain sensory mechanisms decreased
         • Nerve damage
         • Cortical damage
         • High pain thresholds
         • Baseline MS decrease
      ii. Silent / variant ischemic syndromes more common as age increases
         iii. Often present to evaluate complication, not original event
   b. Young
      i. Symptoms often typical
      ii. No age immune
   c. DM
      i. More MIs
      ii. Earlier MIs
      iii. Asymptomatic MIs
      iv. Polyneuropathy
      v. Altered perception cardiac pain
      vi. Extensive comorbidities

4. Prior exams
   a. ‘Negative’ cath
      i. Good for 6-12 mos
      ii. Negative must be truly negative; subcritical 40% lesion could rupture at any time
   b. Negative stress
      i. Reliable for less than 6 mos
      ii. And only 60-70% sensitive for CAD at time of test!
   c. In either case, no result is gold

B. Physical

1. Differential
   a. Pleuritic / positional / palpable
   b. Signs
      i. DVT
      ii. AAA

2. Complications
   i. CHF
   ii. Dysrhythmia
   iii. New murmur
C. Tests

1. EKG
   a. Electrophysiology
      i. Anatomic correlations

<table>
<thead>
<tr>
<th>Anatomic Location</th>
<th>EKG Location</th>
<th>Coronary Artery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septal</td>
<td>V1-2</td>
<td>LAD lesion</td>
</tr>
<tr>
<td>Anterior</td>
<td>V3-4</td>
<td>LAD lesion</td>
</tr>
<tr>
<td>Lateral</td>
<td>V4-6, I, aVL</td>
<td>Circumflex branch of LAD</td>
</tr>
<tr>
<td>Inferior</td>
<td>II, III, aVF</td>
<td>RCA (90%)</td>
</tr>
<tr>
<td>Posterior</td>
<td>V8-9</td>
<td>Circumflex or dominant branch of RCA</td>
</tr>
<tr>
<td>Right Ventricular</td>
<td>V4R</td>
<td>RCA</td>
</tr>
</tbody>
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   ii. Evolution of ischemia
   - ST Depression
   - T wave inversion
   - Biphasic T waves / nonspecific changes
   - Hyperacute T wave
   - ST Elevation / reciprocal depression
   - T wave inversion
   - Q waves

   b. EKG’s of typical localizations of AMI
      i. Anteroseptal STEMI
ii. Anterior STEMI

iii. Anterolateral STEMI

iv. Inferior STEMI
v. Right Ventricular STEMI

vi. Posterior MI

- STD in V1, STE in V8, V9
- pathologic R’s
- R/S ratio > 1 in V1-V2

c. Limitations

   i. **Totally normal EKG: 5% have ACS**
   ii. **Nonspecific: 25% have ACS**
   iii. **50% AMI had nondiagnostic initial EKGs**
   iv. Immediate risk stratification: low
      - Totally normal
      - Nonspecific ST/T wave changes
      - No change
   i. Immediate risk stratification: higher
      - ST deviation
      - Pathologic Q
      - T-wave changes
      - LBBB
      - Pace
      - LVH

d. Confounds and Mimics
i. LBBB
   - Difficult to read EKG for ischemia due to baseline ST changes
   - **Sgarbossa criteria** for diagnosing acute ischemia in face of LBBB
     \[ \rightarrow \text{STE} > 1\text{mm concordant with QRS} = 5 \text{pts} \]
     \[ \rightarrow \text{STD} > 1\text{mm V1, V2, or V3} = 3 \text{pts} \]
     \[ \rightarrow \text{STE} > 5\text{mm discordant with QRS} = 2 \text{pts} \]
   - Score > 3 suggests MI
   - Score < 3 not so clear
   - Presumably new LBBB with clinical MI
     \[ \rightarrow \text{Acute reperfusion therapy} \]
     \[ \rightarrow \text{Historically, LBBB and AMI get less therapy} \]

ii. Paced rhythm
   - Similar to LBBB
     \[ \rightarrow \text{Reverse depolarization} \]
     \[ \rightarrow \text{Mimics and masks} \]
   - Sgarbossa criteria also predict suggest ischemia in paced rhythm—same criteria apply

iii. LVH: Features less suggestive of ischemia
   - Precordial leads V1-V3 should be mirror image of V4-V4
   - Concave ST
   - Asymmetric TWI

iv. Mimics
   - Benign early repolarization
   - **Pericarditis**
   - Left ventricular aneurysm

2. Biomarkers
   a. Creatine Kinase: specifically, CK-MB
      i. MB fraction specific for myocardium
      ii. **Earlier rise**
      iii. Earlier fall
      iv. False positives
         - Trauma
         - Muscular dystrophies
         - Rhabdomyolysis
         - Vigorous exercise
      v. Still need serial testing
   b. Troponin
      i. **Highly sensitive and specific (definitionally)**
      ii. Last longer in the serum
      iii. Predict mortality for all comers
   c. Markers out of favor
      i. Myoglobin
• Very early rise
• Specificity too low
• Does not rule out UA
  ii. New markers—as yet unproven or disproven
    • ST2
    • CRP

3. CXR
   a. **Useful to rule out diagnoses in differential**
      i. Pneumonia
      ii. Pneumothorax
      iii. Rib fracture
      iv. Dissection
   b. Seek out complications
      i. Pulmonary edema
      ii. Cardiomegaly

4. ECHO
   a. Ischemia begins with **hypokinesis**
   b. Progresses to paradoxic akinesis
   c. Relatively cheap and safe
   d. Disadvantages
      i. Not always readily available
      ii. Highly operator dependent
      iii. Cannot differentiate AMI from
          • Noninfarctional ischemia
          • Nontransmural infarction
          • Old infarct

D. Schemata / Protocols

1. Accepted standard: “Rule-out MI”
   a. ED enzymes triage bed type for admit
   b. One to two more sets at q6-8h
   c. **Rule out UA with provocative stress vs. cath**
      i. Provocative factor
         • Exercise
         • Chemical
            → Persantine
            → Dobutamine
      ii. Sensing factor
         • EKG
         • ECHO
         • Nuclear scintography

2. Current Trend: The Chest Pain Unit
   a. Goals
      i. Sensitively and specifically Dx
ii. Decrease utilization by decreasing hospital stays
b. Procedure
   i. Initial risk stratification
   ii. Rapid protocol ROMI
   iii. Stress before D/C
c. Prototype: The Erlanger Protocol
   i. Two hour rule-out
   ii. Initial 5-level risk stratification
   iii. Serial ECG’s q15 minutes
   iv. Comparative delta CK-MB
   v. Re-stratification at 2h
   vi. Stress almost all groups
   vii. Still miss a few ACS
3. Future Goal: Magic Bullet?
   a. Sensitivity approaching 100%
   b. Noninvasive
   c. Cheap
   d. Plentiful
   e. Fast

IV. TREATMENT

A. Management—Goals

1. Reperfuse
   a. Goal of TIMI-3 flow (equal flow before and after lesion)
   b. Outcome data obtained by bench research / tPA
   c. ‘Open Artery Theory’: \textbf{Time = Muscle}
      i. Limit infarct size
      ii. Decreased CHF
      iii. Decreased mortality
   iv. 2 hours is watershed time—\textbf{large benefit if reperfuse $<$ 2h}
      \begin{itemize}
        \item Prehospital delays significant
        \item ED delays less so
           \begin{itemize}
             \item EKG in 10 minutes
             \item Decision time minimization
             \item Action time minimization
           \end{itemize}
        \item Door to drug / balloon
        \item 90 minutes
      \end{itemize}

2. Halt clot formation / progression

3. Decrease current ischemia
   a. Dilate vasculature
   b. Decrease myocardial demand

4. Prevent / treat complications
B. Reperfusion Therapies

1. Thrombolysis
   a. Mechanism
      i. Binds to fibrin-bound plasminogen
      ii. Turns to plasmin
      iii. Plasmin breaks fibrin strands
      iv. Clot busted
   b. Drug Choice
      i. tPA (alteplase, Genentech 1984)
         • Recombinant version of naturally occurring endothelial enzyme
         • Highly fibrin specific
         • ‘Front-load’ 1.5h supplanted old 3h protocol
            → Bolus 15mg
            → .75 mg/kg over next 30 min
            → .5 mg/kg over subsequent 60 minutes
            → Max of 100mg
         • Circulating half-life of 5 minutes
         • Always coadminister IV heparin
      ii. rPA (reteplase, Boeringer 1996)
         • Mutant recombinant tPA
         • Less fibrin-specific
            → Faster
            → Diffuses through entire clot
         • Less bleeding
         • Easier administration
            → ‘Double bolus’ of 10 Units, 30 minutes apart
         • Only inferior to tPA in presentation > 4h
      iii. TNKase (tenecteplase, Genentech 2000)
         • Third-generation mutant (2000)
         • Longer half life: single 30-50mg bolus
         • Extremely fibrin-specific (14x tPA)
         • Outcomes ≥ tPA
      iv. No longer commonly used for ACS
         • Streptokinase
            → Antigenic; allergic reaction common with recent strep infection
            → Inferior outcome data compared to tPA products
         • Urokinase
         • APSAC
   c. Indications: STEMI with EKG showing
      i. STE ≥ 1mm in ≥ 2 contiguous standard limb leads
      OR
      ii. STE ≥ 2mm in ≥ 2 contiguous precordial leads
OR

iii. (presumed) New LBBB
   • Left bundle outcomes worse
   • Treated less frequently
   • Concern for lytic side effects in face of uncertain Dx

d. Absolute contraindications
   i. Active internal bleeding
   ii. CVA history
      • Previous hemorrhagic CVA
      • Ischemic CVA < 1y ago
   iii. Known intracranial mass
      • Neoplasm
      • AVM
      • Aneurysm
   iv. Suspected
      • Aortic dissection
      • Suspected pericarditis

e. Relative contraindications
   i. HTN
      • Acutely > 180/100
      • Chronically uncontrolled
   ii. Old CVA due to intracranial pathology
   iii. INR > 3
   iv. Known bleeding diathesis
   v. Trauma < 2 wks
   vi. CPR > 10 min
   vii. Major surgery < 3 wks
   viii. Noncompressible vascular puncture
   ix. Internal bleed < 4 wks
   x. Pregnancy
   xi. Active PUD

f. Complications
   i. Bleeding
   ii. Allergy (streptokinase)

2. PCI / PTCA
   a. Background
      i. Mechanical revascularization
      ii. Balloon expansion of arterial lumen
      iii. Greater dilatation gives
         • Less restenosis
         • More complications: dissection, thrombus, rupture
      iv. Often leave fenestrated stent as scaffold
   b. Has become industry standard
      i. Primary PTCA: outcomes better than lytics, IF
         • Performed within time window (90-120 min)
• Performed by experienced operator
  ii. Need to have staffing / backup
  iii. Less bleeding complications
  iv. **Hard indication for cardiogenic shock**

3. Combinations
   a. Rescue angioplasty
      i. Diagnostic: check flow after lytics (rarely used)
      ii. Therapeutic: mechanically dilate artery if not resolved after lytics
   b. Facilitated PCI
      i. Half-dose front-load tPA or other lytic followed by cath
      ii. Used if PCI imminent, but expecting delay past 90 min
      iii. Shown to be both safe and effective

4. Emergent CABG
   a. Last resort
   b. Failed PCI with continued symptoms / instability

C. Anticoagulants / Antiplatelets

1. Aspirin
   a. Features
      i. Potent irreversible antiplatelet
      ii. Cheap
      iii. Extremely effective
         • **Alone decreases mortality 23%**
         • Synergizes with lytics (42% mortality reduction)
   b. Dosages
      i. 160mg - 325mg
      ii. Chewed preferable (faster onset)
   c. Contraindications
      i. Acute GI bleed
      ii. Allergy to ASA (use Plavix)

2. Plavix (clopidogrel)
   a. Inhibits GP IIb/IIIa transformation to high-affinity state
   b. Routine ED use not proven
   c. Credible antiplatelet **backup in ASA allergy** (300mg load)

3. GPIIb/IIIa inhibitors
   a. Mechanism
      i. Inhibits receptor on surface of platelet
      ii. Prevents crosslinking of fibrinogen / vWF
      iii. Therefore decreases platelet adhesion
   b. Drug choices
      i. Eptifibatide (Integrillin)
      ii. Tirofiban (Aggrastat)
      iii. Abciximab (try saying several times in a row) (ReoPro)
   c. Indications
i. **Improves outcome if PCI performed**

ii. Some centers using routinely for all MI

4. Heparins
   a. Mechanism
      i. Binds antithrombin III, eventually preventing fibrin formation
      ii. Stops new clot formation
         - Keeps newly revascularized arteries patent (a necessity when using lytics)
         - Prevents mural thrombus formation in anterior MI
         - Prevents formation and dissemination of clots to CNS
         - **Does nothing to break up existing clot**
         - **Indicated in UA and MI**
   b. Unfractionated heparin
      i. Load at 60 U/kg, infuse at 12 U/kg/hr
      ii. Max of 5000 U bolus / 1000 U/hr
      iii. Goal of PTT 1.5 to 2.5 times control
   c. Low molecular weight heparins
      i. Inactivates factor Xa
      ii. Equal or greater efficacy to UFH
         - Not all LMWH are the same
         - Literature supports Lovenox (enoxaparin) over others
      iii. Easier to administer, less frequent checks, fewer complications: overall cheaper
      iv. Indicated in UA, used often.
      v. Not routinely used in AMI: many interventionalists loath subsequent cath (long half-life, unclear reversal characteristics)

D. Maximize oxygen delivery / minimize oxygen consumption

1. Nitrates: nitroglycerin
   a. Decrease preload and dilate coronary vasculature
      i. **Contraindicated in hypotension below 90mm syst**
      ii. **Seriously consider holding in inferior/RV infarct, as decreasing preload may induce severe hypotension**
   b. Historically shows some mortality benefit in AMI
   c. Three SL’s followed by IV
      i. Start at 10 ug/min
      ii. Titrate until pain free, max 200

2. Beta adrenergic blockade
   a. Decrease myocardial oxygen demand
      i. Decrease catechol-induced tachycardia
      ii. Decrease contractility
   b. **Contraindications**
      i. Severe COPD / asthma
ii. CHF
iii. Bradycardia / AV nodal blockade
iv. Hypotension
v. Contraindications may explain why this proven therapy is often not given in clinical situations
c. Any β-Blocker will do
   i. Most commonly metoprolol 5mg IV
   ii. Esmolol gtt is ultra-short acting, consider in presence of contraindications

3. Opioid analgesia
   a. Theoretically decreased myocardial O\textsubscript{2} consumption by decreasing pain and anxiety
   b. Some vasodilatory effects
   c. Never proven in trials
   d. Why not?

4. Oxygen
   a. Goal is to maximize O\textsubscript{2} delivery
   b. Attempt to maximize PaO\textsubscript{2}

E. Treat complications
1. Antiarrhythmics: **routine administration not indicated**
2. Pressors
   a. Begin with fluids, especially in RV infarct syndromes
   b. Each vasoactive has its indications and side effects
c. Norepinephrine
   i. Increases SVR
   ii. Indicated in hypotension below 80mm systolic
   iii. Increased myocardial O\textsubscript{2} demand
   iv. Switch to dopamine when you hit 80
d. Dopamine
   i. Vasoactive of choice above 80mm systolic
   ii. Increases HR, but overall best profile of the vasoactives in face of MI
e. Dobutamine
   i. Can consider coadministration with DA above 90mm systolic to decrease amount of DA needed
   ii. Dilates coronary vasculature
   iii. Less myocardial O\textsubscript{2} demand than others

3. Mechanical intervention
   a. Endotracheal intubation
   b. Intraaortic balloon pump
      i. Used in refractory cardiogenic shock
      ii. Inflates in diastole, deflates for systole
      iii. Vacuum assists LV
      iv. Overall improves CO and EF, increases coronary perfusion pressure, and decreases myocardial O\textsubscript{2} demand
ACUTE CORONARY SYNDROMES

PEARLS

1. ACS is common, and the cause of large amounts of morbidity, mortality, and litigation.

2. UA is any change in symptoms from that patient’s previous baseline.

3. Acute MI is now defined mainly by an increase in serum troponin.

4. Incompletely occlusive white thrombus is thought to cause UA, completely occlusive red thrombus is thought to cause AMI.

5. Typical anginal symptoms include exertional squeezing/choking and shortness of breath.

6. ‘Atypical’ anginal equivalents are extremely common, especially in the old and diabetic.

7. Prior stress / cath results are of limited use in ‘ruling out’ ACS in the ED.

8. EKG is the foremost risk-stratification and diagnostic tool for ACS, but alone cannot ‘rule out’ MI/UA.

9. Consider concordance and the Sgarbossa criteria in evaluation for ischemia in the face of LBBB or paced rhythm.

10. Cardiac enzymes are the standard for ruling-in MI, but one set never rules it out.

11. The goal for reperfusion of AMI is 90 minutes, whether by balloon or chemical.

12. Don’t forget ASA, heparin, and β-blocker unless they are contraindicated—all have a significant mortality benefit in AMI.
REFERENCES


