Acute Coronary Syndrome

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Objectives

1. understand the mechanisms and pathophysiology of acute coronary syndromes
2. be able to rapidly identify high risk and low risk ACS patients
3. discuss current pharmacologic and interventional treatment modalities for ACS
Definitions
Definitions - Biological

Most commonly:
- ruptured plaque
- non-occlusive, platelet-rich thrombus
- distal microembolization

Also may have:
- spasm
- anemia
- tachyarrhythmias
- HTN (high LVEDP)
Goals of Tx

Short Term:
- Address acute hemodynamic status
- Pain relief
- Prevention of acute thrombosis/embolism
- Prevention of arrythmias

Long Term:
- Slow progression of disease
- Prevent future events (death, MI, rehosp, revasc)
- Prevention of angina
Early Clinical Assessment

- Traditional risk factors only weakly predictive of ACS
  - Do predict worse prognosis once ACS has been established

- Clinical symptoms, ECG, biomarkers much more predictive
Early Clinical Assessment

- Atypical symptoms do not necessarily decrease the likelihood of ACS
    - Sharp or stabbing pain --> 22% had acute ischemia
    - Pleuritic pain --> 13% had acute ischemia
    - Pain reproduced with palpation --> 7% had acute ischemia

- Older age, male sex, presence of chest or left arm pain, chest pain identified as most important presenting symptom all increase the likelihood of ACS (N Engl J Med 1984;310:1273-8; Med Care 1991;29:610-27)
Early Clinical Assessment

ECG

- ECG changes define a gradient of risk
  - BBB, paced rhythm, LVH with repol
    (“uninterpretable” ECGs)
  - ST segment deviation
  - T wave inversions ≥ 0.2mV
  - Non-specific T wave abnormalities or normal ECG
Early Clinical Assessment

ECG

Figure 19. Kaplan-Meier Estimates of Probability of Death Based on Admission Electrocardiogram
CLASS I

1. In patients with chest pain or other symptoms suggestive of ACS, a 12-lead ECG should be performed and evaluated for ischemic changes within 10 minutes of the patient arrival at an emergency facility (21). (Level of Evidence: C)

2. If the initial ECG is not diagnostic but the patient remains symptomatic and there is a high clinical suspicion for ACS, serial ECGs (e.g., 15- to 30-minute intervals during the first hour) should be performed to detect ischemic changes. (Level of Evidence: C)
Biomarkers (BNP)

Mortality at 10 mo (%)

- ST ↑ MI
  - Q1: 825
  - Q2: 565
  - Q3: 1133
  - P = .02

- Non-ST ↑ MI
  - Q1: 825
  - Q2: 565
  - Q3: 1133
  - P < .0001

- Unstable Angina
  - Q1: 825
  - Q2: 565
  - Q3: 1133
  - P = .001

Biomarkers (troponin, CRP, BNP)

OPUS-TIMI 16

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TACTICS-TIMI 1

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The Sanchis score (49), Vancouver rule (50), Heart (History, ECG, Age, Risk Factors, and Troponin) score (51), HEARTS3 score (52), and Hess prediction rule (53) were developed specifically for patients in the ED with chest pain. Although no definitive study has demonstrated the superiority of risk assessment scores or clinical prediction rules over clinician judgment, determination of the level of risk on initial evaluation is imperative to guide patient management, including the need for additional diagnostic testing and treatment. See Section 3.2.2 for a discussion of risk stratification variables.
TIMI Risk Score

1) Age ≥65 years
2) ≥3CAD Risk Factors
3) Prior Stenosis >50%
4) ST deviation
5) ≥2 Anginal events <24 hours
6) ASA in last 7 days
7) Elev Cardiac Markers (CK-MB or troponin)

D/MI/Urg Revasc (%) at 14ds

Number of Risk Factors

Population (%): 4.3 17.3 32.0 29.3 13.0 3.4

Pharmacological Therapy
antiplatelet agents

- ASA
  - 325mg chewed
  - 81mg if taking Ticagrelor or Prasugrel

- Clopidogrel or Ticagrelor (Prasugrel only after PCI)
  - loading dose
  - delays CABG by 5ds

- IIB/IIIA inhibitors
  - highest risk cohort, ongoing ischemia
  - most benefit if early PCI planned
### TABLE 7
Summary of Recommendations for Initial Antiplatelet/Anticoagulant Therapy in Patients With Definite or Likely NSTE-ACS and PCI

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Dosing and Special Considerations</th>
<th>COR</th>
<th>LOE</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aspirin</strong></td>
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<tr>
<td>• Non-enteric-coated aspirin to all patients promptly after presentation</td>
<td>162 mg–325 mg</td>
<td>I</td>
<td>A</td>
<td>(288-290)</td>
</tr>
<tr>
<td>• Aspirin maintenance dose continued indefinitely</td>
<td>81 mg/d–325 mg/d*</td>
<td>I</td>
<td>A</td>
<td>(288-290, 293,391)</td>
</tr>
<tr>
<td><strong>P2Y12 inhibitors</strong></td>
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<tr>
<td>• Clopidogrel loading dose followed by daily maintenance dose in patients unable to take aspirin</td>
<td>75 mg</td>
<td>I</td>
<td>B</td>
<td>(291)</td>
</tr>
<tr>
<td>• P2Y12 inhibitor, in addition to aspirin, for up to 12 mo for patients treated initially with either an early invasive or initial ischemia-guided strategy: Clopidogrel, Ticagrelor</td>
<td>300-mg or 600-mg loading dose, then 75 mg/d</td>
<td>I</td>
<td>B</td>
<td>(289,292)</td>
</tr>
<tr>
<td>• P2Y12 inhibitor therapy (clopidogrel, prasugrel, or ticagrelor) continued for at least 12 mo in post-PCI patients treated with coronary stents</td>
<td>180-mg loading dose, then 90 mg BID</td>
<td></td>
<td></td>
<td>(293,294)</td>
</tr>
<tr>
<td>• Ticagrelor in preference to clopidogrel for patients treated with an early invasive or ischemia-guided strategy</td>
<td>N/A</td>
<td>Ila</td>
<td>B</td>
<td>(293,294)</td>
</tr>
<tr>
<td><strong>GP IIb/IIIa inhibitors</strong></td>
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<tr>
<td>• GP IIb/IIIa inhibitor in patients treated with an early invasive strategy and DAPT with intermediate/high-risk features (e.g., positive troponin)</td>
<td>Preferred options are eptifibatide or tirofiban</td>
<td>Ilb</td>
<td>B</td>
<td>(43,94,295)</td>
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<tr>
<td><strong>Parenteral anticoagulant and fibrinolytic therapy</strong></td>
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<tr>
<td>• SC enoxaparin for duration of hospitalization or until PCI is performed</td>
<td>1 mg/kg SC every 12 h (reduce dose to 1 mg/kg/d SC in patients with CrCl &lt;30 mL/min)</td>
<td>I</td>
<td>A</td>
<td>(133,138,309)</td>
</tr>
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<td>• Loading dose 0.10 mg/kg loading dose followed by 0.25 mg/kg/h</td>
<td>(292,293, 310,311)</td>
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<tr>
<td>• Bivalirudin until diagnostic angiography or PCI is performed in patients with early invasive strategy only</td>
<td></td>
<td>I</td>
<td>B</td>
<td>(292,293, 310,311)</td>
</tr>
</tbody>
</table>
GP IIb/IIIa Antagonists in ACS: Death or MI at 30 Days in PCI/CABG < 5 Days Cohort vs Medical Treatment Cohort

ACS, acute coronary syndrome; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; NS, not significant.
Pharmacological Therapy
antithrombotic agents

- Heparin
  - Easiest to reverse
- LMWH
  - Easiest to dose
  - Less HIT
- Direct thrombin inhibitors (lepirudin, bivalrudin, etc.)
  - For pts with HIT
Figure 10. Older Trials of Antiplatelet and Anticoagulant Therapy in UA/NSTEMI
Pharmacological Therapy
Nitrates

- **benefits**
  - pain, HTN, decrease preload
  - no documented mortality benefit

- reflex increase in HR and contractility
  - should be used with beta blockers

- **contraindications**
  - severe AS, RV infarct, recent sildenafil
Pharmacological Therapy
Beta Blockers

- Benefits
  - ↓ MVO2, ↑ diastolic coronary perfusion
- IV (5mg IV Q5min X 3)
- PO (12.5-25mg PO Q6 X 48hrs)
- BID dosing for maintenance outpt tx
- Caution in LV dysfunction, active heart failure, shock/low-output

- Most data from AMI, chronic stable angina, s/p recent MI, heart failure.
  - Little data specifically in ACS
Pharmacological Therapy
Calcium Channel Blockers

- May use diltiazem or verapamil acutely for pts in whom beta blockers are contraindicated

- Caution in LV dysfunction

- Short-acting dihydropyridines without beta blockade showed increased events
Early invasive vs conservative

Conservative
No. of Patients: 920

Invasive
1674

No. of Patients: 7018

- VANQWISH
- MATE
- TIMI IIIb
- ISAR-COOL
- RITA-3
- VINO
- TRUCS
- TACTICS-TIMI 18
- FRISC II
Early invasive vs conservative

TACTICS - TIMI 18

TnT, troponin T; ST, ST segment.
Case 1

- 72yo male h/o HTN, hyperchol, AF, COPD, DM, LVEF 45%, mod MR
- CP rad L arm, R arm, jaw, assoc with SOB, nauaeae, several hours off and on
- Insulin, lasix, dig, quinapril, simva, warfarin
- Trop 0.05, 1.64, 1.97, 1.52
Case 1

- Tx with Lovenox, metoprolol, clopidogrel
- 95% LCx lesion, successful PCI
Case 2

- 34yo male h/o STEMI s/p PCI 2yrs ago, uses “spice,” med noncompliance
- CP while wrestling with his dogs, central chest, sharp, radiated to neck, waxed/waned few hours
- Trop 0.05, 1.64, 1.97, 1.52
Case 2

- Tx with metoprolol, asa, clopidogrel, atorva
- Cath showed patent stent, normal LVEF, no PCI done
Case 3

- 84yo female h/o CAD s/p PCI, DM, HTN, CVA, CKD, recent echo with nl LVEF
- c/o inc SOB past 2 wks, worse this AM, + orthopnea and PND
- asa, carvedilol, clopidogrel, furosemide, isosorbide, rosuvastatin, losartan, insulin
- Trop 0.16, 0.14
- NT-proBNP 58,358
- Cr 1.9
Case 3

- Tx with diuretics
- Stress test showed scar without ischemia
- No cath done
Case 4

- 89 yo male h/o CAD s/p PCI, HTN, hyperchol, RA, is a “DNR”
- CP past 3 wks, several times per day, relieved with NTG, radiates shoulders/arms, both exertional and at rest, neg stress test at VA 8 wks ago
- asa, dilt, isosorbide, metoprolol, prava, mtx
- Trop 0.08, 0.09, 0.11
Case 4

- Tx with clopidogrel, atorva
- Stress test with anterior and lateral ischemia
- Cath showed severe stenosis of distal LM, ostial LCx, prox-mid LAD. Surgical opinion obtained, Tx with multivessel PCI