ACUTE CORONARY SYNDROMES: NSTEMI NOT NONEMERGENT

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October 12, 2016
DISCLOSURES

Speakers bureau for:
Medtronic
Acute Coronary Syndromes

All are characterized by plaque rupture and coronary thrombosis.

- **Unstable Angina**
  - Vessel not occluded in 80% of cases

- **NSTEMI**

- **STEMI**
  - Vessel is occluded in 80% of cases
Unstable angina

- Diagnosis based on ischemic symptoms at rest without elevation in troponin.
NSTEMI

- Diagnosis based on ischemic symptoms with an elevation in troponin.
Troponin T and I

*(-+) transient ischemic or inflammatory myocardial injury. Thus, may be detected in conditions other than ACS.

* heart failure,
* cardiomyopathies

* myocarditis,
* renal failure,
* tachyarrhythmias
* pulmonary embolism
* strenuous exercise in healthy individuals.
Acute Coronary Syndrome

High-sensitivity assays

- cTn Assay
  - TnI
  - cTnI
  - TnI-Ultra

- Diagnostic cutoff
  - \( \geq 1.5 \text{ ng/mL} \)
  - \( > 0.10 \text{ ng/mL} \)
  - \( > 0.04 \text{ ng/mL} \)

- Implementation
  - 1995
  - 2003
  - 2007
Myocardial infarction classification

<table>
<thead>
<tr>
<th>Class 1</th>
<th>Spontaneous MI related to ischemia due to a primary coronary event, such as plaque erosion and/or rupture, fissuring, or dissection</th>
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</thead>
<tbody>
<tr>
<td>Class 2</td>
<td>MI secondary to ischemia due to an imbalance of O2 supply and demand, as from coronary spasm or embolism, anemia, arrhythmias, hypertension, or hypotension</td>
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<tr>
<td>Class 3</td>
<td>Sudden unexpected cardiac death, including cardiac arrest, often with symptoms suggesting ischemia with new ST-segment elevation; new left bundle branch block; or pathologic or angiographic evidence of fresh coronary thrombus—in the absence of reliable biomarker findings.</td>
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<tr>
<td>Class 4a</td>
<td>MI associated with PCI</td>
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<tr>
<td>Class 4b</td>
<td>MI associated with documented in-stent thrombosis</td>
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<tr>
<td>Class 5</td>
<td>MI associated with CABG surgery</td>
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</tbody>
</table>
90 year old woman recently admitted at another facility where POBA was performed on RCA. Is having refractory angina

Troponin elevated on admission to 0.032 (ULN 0.028)
72 year old with syncope, fever, elevated WBC and shortness of breath

Troponin 2.30 (ULN 0.028)
82 year old lady with exertional fatigue, SOB, and acute on chronic systolic CHF. Creat 1.9. Stasis ulceration on both legs.

Troponin 5.4 (ULN 0.028)
• LAD 90% and Cx 90% on angio
• Invasive AV mean gradient was 48mmHg
Troponin level and mortality
74 year old male

- Presents to the clinic with exertional chest pain for the past month.
- Had been seen at a community ER one month prior
  - ECG normal
  - Troponin 0.13
  - History of tobacco abuse
  - Hypercholesterolemia
  - Given imdur and released to home without noninvasive stress testing
ND may have a problem

- Question: Are ACS patients falling through the cracks in our smaller communities?
- Has the emphasis on STEMI de-emphasized UA/NSTEMI?

Ezra A. Amsterdam, Nanette K. Wenger, Ralph G. Brindis, Donald E. Casey, Jr., Theodore G. Ganiats, David R. Holmes, Jr., Allan S. Jaffe, Hani Jneid, Rosemary F. Kelly, Michael C. Kontos, Glenn N. Levine, Philip R. Liebson, Debabrata Mukherjee, Eric D. Peterson, Marc S. Sabatine, Richard W. Smalling and Susan J. Zieman
Nomenclature

- NSTEMI + Unstable angina = NonST elevation ACS
- Troponin negative or troponin positive NonST elevation ACS
- Conservative mgt = ischemia guided strategy
Chest pain suggestive of ACS -- Class I

- **Early risk stratification** -- Likelihood of CAD/events
- **ECG** within 10 min, and q 15-30 min if symptomatic
- **Biomarkers** - Troponin is preferred
Class III: No Benefit

1. An early invasive strategy (i.e., diagnostic angiography with intent to perform revascularization) is not recommended in patients with:
   a. Extensive comorbidities (e.g., hepatic, renal, pulmonary failure, cancer), in whom the risks of revascularization and comorbid conditions are likely to outweigh the benefits of revascularization. (Level of Evidence: C)
   b. Acute chest pain and a low likelihood of ACS (Level of Evidence: C) who are troponin-negative, especially women (178). (Level of Evidence: B)

Invasive strategy not recommend
- when revascularization will not benefit the patient
- When ACS is not likely and troponin negative
All others benefit from invasive strategy

Class I

1. An urgent/immediate invasive strategy (diagnostic angiography with intent to perform revascularization if appropriate based on coronary anatomy) is indicated in patients (men and women) with NSTE-ACS who have refractory angina or hemodynamic or electrical instability (without serious comorbidities or contraindications to such procedures) (40, 42, 173, 174). *(Level of Evidence: A)*

2. An early invasive strategy (diagnostic angiography with intent to perform revascularization if appropriate based on coronary anatomy) is indicated in initially stabilized patients with NSTE-ACS (without serious comorbidities or contraindications to such procedures) who have an elevated risk for clinical events (Table 8) (40, 42, 173-177). *(Level of Evidence: B)*

Class IIa

1. It is reasonable to choose an early invasive strategy (within 24 hours of admission) over a delayed invasive strategy (within 24 to 72 hours) for initially stabilized high-risk patients with NSTE-ACS. For those not at high/intermediate risk, a delayed invasive approach is reasonable (173). *(Level of Evidence: B)*

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Refractory angina, Hemodynamic instability, Mod/high risk
**NSTE-ACS: Definite or Likely**

- **Ischemia-Guided Strategy**
  1. **Initiate DAPT and Anticoagulant Therapy**
     - ASA (Class I; LOE: A)
     - P2Y\(_{12}\) inhibitor (in addition to ASA) (Class I; LOE: B):
       - Clopidogrel or
       - Ticagrelor
     - Anticoagulant:
       - UFH (Class I; LOE: B) or
       - Enoxaparin (Class I; LOE: A) or
       - Fondaparinux (Class I; LOE: B)

- **Early Invasive Strategy**
  1. **Initiate DAPT and Anticoagulant Therapy**
     - ASA (Class I; LOE: A)
     - P2Y\(_{12}\) inhibitor (in addition to ASA) (Class I; LOE: B):
       - Clopidogrel or
       - Ticagrelor
     - Anticoagulant:
       - UFH (Class I; LOE: B) or
       - Enoxaparin (Class I; LOE: A) or
       - Fondaparinux (Class I; LOE: B) or
       - Bivalirudin (Class I; LOE: B)
  2. Can consider GPI in addition to ASA and P2Y\(_{12}\) inhibitor in high-risk (e.g., troponin positive) pts (Class IIb; LOE: B)
     - Eptifibatide
     - Tirofiban
Ischemia guided pathway

- Guideline directed medical therapy
- Noninvasive LV function evaluation— Echo
- Stress testing if asymptomatic after 12-24 hours of hospital evaluation with low level activity
Invasive strategy

- Guideline directed medical therapy
- Coronary angiography
  - Immediate invasive
  - Early invasive
  - Delayed invasive
<table>
<thead>
<tr>
<th>Immediate invasive (within 2 h)</th>
<th>Refractory angina</th>
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<tbody>
<tr>
<td></td>
<td>Signs or symptoms of HF or new or worsening mitral regurgitation</td>
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<td></td>
<td>Hemodynamic instability</td>
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<td></td>
<td>Recurrent angina or ischemia at rest or with low-level activities despite intensive medical therapy</td>
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<thead>
<tr>
<th>Ischemia-guided strategy</th>
<th>Sustained VT or VF</th>
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<tr>
<td></td>
<td>Low-risk score (e.g., TIMI [0 or 1], GRACE [&lt;109])</td>
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<td>Low-risk Tn-negative female patients</td>
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<td></td>
<td>Patient or clinician preference in the absence of high-risk features</td>
</tr>
</tbody>
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<thead>
<tr>
<th>Early invasive (within 24 h)</th>
<th>None of the above, but GRACE risk score &gt;140</th>
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<tbody>
<tr>
<td></td>
<td>Temporal change in Tn (Section 3.4)</td>
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<td></td>
<td>New or presumably new ST depression</td>
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<thead>
<tr>
<th>Delayed invasive (within 25–72 h)</th>
<th>None of the above but diabetes mellitus</th>
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<tr>
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<td>Renal insufficiency (GFR &lt;60 mL/min/1.73 m²)</td>
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<td></td>
<td>Reduced LV systolic function (EF &lt;0.40)</td>
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<td></td>
<td>Early postinfarction angina</td>
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<td></td>
<td>PCI within 6 mo</td>
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<td></td>
<td>Prior CABG</td>
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<tr>
<td></td>
<td>GRACE risk score 109–140; TIMI score ≥2</td>
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RISK STRATIFICATION
Sensitivity vs Specificity

Our history and physical as a diagnostic test

Sensitive
Miss no one
Include everyone

Specific
Miss a lot
Include only those with definite CAD
## Clinical Assessment

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Typical CP</th>
<th>Atypical CP</th>
<th>Noncardiac CP</th>
</tr>
</thead>
<tbody>
<tr>
<td>30+</td>
<td>Male</td>
<td>Intermediate</td>
<td>Intermediate</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>Intermediate</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>40+</td>
<td>Male</td>
<td>High</td>
<td>Intermediate</td>
<td>Intermediate</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>Intermediate</td>
<td>Low</td>
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</tr>
<tr>
<td>50+</td>
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<td>High</td>
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</tr>
<tr>
<td></td>
<td>Female</td>
<td>High</td>
<td>Intermediate</td>
<td>Intermediate</td>
</tr>
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</table>
TIMI Risk Score

- Age > 65
- Presence of 3 or more risk factors for CAD
  - HTN, HC, DM, Tobacco, FH of early MI
- ST deviation on initial ECG
- Known coronary stenosis > 50%
- Prior anginal episodes in last 24 hrs
- Elevated biomarkers
- Prior use of aspirin
What does a higher score mean?

Risk of MACE through 14 days

- Low: 0-1
- Medium: 2, 3
- High: 4, 5, 6-7

TIMI Score
IMMEDIATE MANAGEMENT
Patients with suspected ACS and high-risk features such as continuing chest pain, severe dyspnea, syncope/presyncope, or palpitations should be referred immediately to the emergency department (ED) and transported by emergency medical services when available.
- ECG within 10 minutes with repeats every 15-30 minutes with continued symptoms
- Troponin level with repeat in 3 - 6 hours
- Risk scores should be utilized
3.4.1. Biomarkers: Diagnosis

Class I

1. Cardiac-specific troponin (troponin I or T when a contemporary assay is used) levels should be measured at presentation and 3 to 6 hours after symptom onset in all patients who present with symptoms consistent with ACS to identify a rising and/or falling pattern (22, 43-48, 70-74). *(Level of Evidence: A)*

2. Additional troponin levels should be obtained beyond 6 hours after symptom onset in patients with normal troponins on serial examination when electrocardiographic changes and/or clinical presentation confer an intermediate or high index of suspicion for ACS (22, 49-51, 75). *(Level of Evidence: A)*

3. If the time of symptom onset is ambiguous, the time of presentation should be considered the time of onset for assessing troponin values (44, 45, 49). *(Level of Evidence: A)*
HOSPITAL CARE
Standard medical therapies

- Aspirin
- Ticagrelor or Plavix
- Anticoagulant (heparin, enox, bival, fonda)
- Nitrate
- Morphine
- Beta blockers
- CCB if BB contraindicated
- HIST
- ACE if LVEF <40%, HTN, DM sCKD
…to observe patients with nonischemic initial ECG and normal cardiac troponin in a chest pain unit with serial ECGs and cardiac troponin at 3- to 6-hour intervals (90-94). (Level of Evidence: B)

…for patients with possible ACS who have normal serial ECGs and cardiac troponins to have stress testing before discharge or within 72 hours after discharge or coronary CTA. (Level of Evidence: B)
How risk affects treatment?

* Invasive
  - Recurrent angina or ischemia at rest or with low-level activities despite intensive medical therapy
  - Elevated cardiac biomarkers (TnT or TnI)
  - New or presumably new ST-segment depression
  - Signs or symptoms of HF or new or worsening mitral regurgitation
  - High-risk findings from noninvasive testing
  - Hemodynamic instability
  - Sustained ventricular tachycardia
  - PCI within 6 months

* Prior CABG
  - High risk score
  - Reduced left ventricular function (LVEF less than 40%)

* Ischemia guided
  - Low risk score
  - Patient or physician preference in the absence of high-risk features

* IIB/IIIA use “may be” reasonable in high risk patients.
Patient #1

- 42 year old white female with chest pain present since yesterday.
- Radiates to arms and back
- States her Dad had MI at 70 y/o. 3 months ago.
- Exercises 3x/week.
- Negative ECG and biomarkers.
Patient #2

- 42 year old white female with chest pain present since yesterday.
- Radiates to arms and back
- States her Dad had MI at 70 y/o. 3 months ago.
- Exercises 3x/week.
- Negative ECG
- Troponin 0.40
Patient #3

- 56 year old NAM
- Smoker, HC, HTN
- Chest pain for 10 minutes this morning after breakfast.
- Took his breath away
- Abdominal obesity
- Exertional symptoms over the last week
- Nonspecific changes on ECG
- Neg biomarkers.
Case #4

🌟 66 year old white male presents with chest pain at rest and lasted 15 minutes. He states that he had a similar episode yesterday.

🌟 PMH- HTN, DM  FH + for CAD

🌟 Meds- ASA, ACE, Metformin   Exam normal

🌟 Troponin 0.40

🌟 ECG showed ST depression in avL, V5, V6
Subsequent management

- Low risk patients may be referred for outpatient stress testing within 72 hours of discharge if ECG and biomarkers are negative after 12 hour observation.

- Not low risk patients should ideally be referred for angiography. They may undergo stress testing if EF is above 40% and they are clinically stable.
Subsequent management

- Patients may be managed medically if stress testing results in low risk scan.
- Patients with not low risk scans should be referred for invasive rx.
Beware of coexistent symptoms

- Shortness of breath
- Syncope
- Continued chest pain
What is high risk

- Bruce Treadmill: ST deviation at low workload, ST elevation, Drop in BP with exercise.
- Stress SPECT: 2 or more vascular territories, TID, drop in EF with stress
- Stress echo: 2 or more vascular territories, drop in EF with stress.
When to hold or transfer

- Hold -- Low risk patients.
- Transfer – Moderate - high risk patients.
DAPT GUIDELINES
Stable ischemic Heart disease

- Patients with a history of acute coronary syndrome greater than one year prior to have since remained free of recurrent ACS are considered to have transitioned to stable ischemic heart disease.
DAPT study

- Studied do antiplatelet therapy--12 months versus 30 months
  - 0.7% absolute reduction in very late stent thrombosis
  - 2% absolute reduction in MI
  - 0.9% absolute increase in moderate for severe bleeding
DAPT subgroup analysis

- 0.4% absolute reduction in stent thrombosis
- 1.1% absolute reduction in MI
- 1.2% absolute increase in moderate to severe bleeding

Weighted risk benefit analysis found 6 fewer MIs, 3 fewer stent thrombosis but 5 additional major bleeds per 1000 patients treated with prolonged dual antiplatelet therapy.
Randomized patients with established atherosclerosis for high risk of clinical atherosclerotic disease to dual antiplatelet therapy or aspirin monotherapy.

No difference in the ischemic events at 28 months 0.4% absolute increase in bleeding
PEGASUS-TIMI-54

- Randomized 1 to 3 years after myocardial infarction to Ticagrelor or aspirin alone
- After 33 months there was a 1.2% absolute reduction in primary endpoint and 1.2% increase in major bleeding but no excess fatal or intracranial bleeding.
Antiplatelet therapy

- Aspirin 81 mg recommended with DAPT
- Ticagrelor given IIa recommendation over Clopidogrel for ACS
DAPT therapy in Stable ischemic heart disease

CLASS I
BMS 1 month of plavix (I)
DES 6 months of plavix(I)

CLASS IIb
BMS > 1 month (If no excess bleeding risk)
DES > 6 months (If no excess bleeding risk)
DES < 3 months (if increased bleeding risk)
DAPT therapy in Acute coronary syndrome

- **Class I**
  - DES or BMS 1 year

- **Class IIa**
  - Ticagrelor favored over plavix
  - Prasugrel favored over plavix (If no bleeding risk or h/o stroke/TIA)

- **Class IIb**
  - DAPT <6 months or >12 months
Figure 1. Master Treatment Algorithm for Duration of P2Y₁₂ Inhibitor Therapy in Patients With CAD Treated With DAPT
Patients Treated With PCI Undergoing Elective Noncardiac Surgery

BMS treated with DAPT

0 d

30 d

<30 d since BMS implantation

Class III: Harm
Delay surgery

≥30 d since BMS implantation

Class I: Proceed with surgery

3 mo

<3 mo since DES implantation

Class III: Harm
Delay surgery

3-6 mo since DES implantation

Class IIb:
Proceeding with surgery may be considered

6 mo

≥6 mo since DES implantation, discontinue DAPT

Class I:
Proceed with surgery
THANK YOU