ACEP Clinical Policy:
Critical Issues in the Evaluation and Management of Emergency Department Patients With Suspected Non–ST-Elevation Acute Coronary Syndromes

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PROBLEM

- Miss up to 2% of acute MIs
- Improving miss rates, but increased:
  - False positives
  - LOS in ED
  - Excessive testing
OUTCOME
30 D MACE

- CARDIOVASCULAR DEATH
- MYOCARDIAL INFARCTION
- REVASCULARIZATION
QUESTIONS

• In adult patients without evidence of ST-elevation ACS, can initial risk stratification be used to predict a low rate of 30-day MACE?

• In adult patients with suspected acute NSTE ACS, can troponin testing within 3 hours of ED presentation be used to predict a low rate of 30-day MACE?

• In adult patients with suspected NSTE ACS in whom acute MI has been excluded, does further diagnostic testing for ACS prior to discharge reduce 30-day MACE?

• Should adult patients with acute NSTEMI receive immediate antiplatelet therapy in addition to aspirin to reduce 30-day MACE?
In patients with chest pain what is an acceptable miss rate for MACE at 30 days?

- 0% = what we really want
- 1% = what we accept
- 2% ≈ test threshold
- 5% = what some patients accept

BMC Medical Informatics and Decision Making 2005, 5:26
1. In adult patients without evidence of ST-elevation ACS, can initial risk stratification be used to predict a low rate of 30-day MACE?

- **Level B recommendations.** In adult patients without evidence of ST-elevation ACS, the History, ECG, Age, Risk factors, Troponin (HEART) score can be used as a clinical prediction instrument for risk stratification. A low score (≤3) predicts 30-day MACE miss rate within a range of 0% to 2%.

- **Level C recommendations.** In adult patients without evidence of ST-elevation ACS, other risk-stratification tools, such as Thrombolysis in Myocardial Infarction (TIMI), can be used to predict rate of 30-day MACE.
TIMI = 0

- Sensitivity overall
  - 67 to 100%
- High Sensitivity Troponin
  - 98.4 % [95.9 to 99.4]
  - 100 % [94.3 to 100]
  - 100 % [91.6 to 100]
COMPARISON: Conventional Troponins

- TIMI = 0 (n = 434)
  - Sensitivity 100% [95% C.I. 94.3 – 100]
  - Specificity 8.5% [95% C.I. 5.9 – 12.0]

- HEART ≤ 2 (n=374)
  - Sensitivity 92.8% [95% C.I. 83.2 – 97.3]
  - Specificity 43.6% [95% C.I. 38.0 – 49.4]

High Sensitivity Troponin (hs-Tn)

- Detect troponin at levels 10- to 100-fold lower than contemporary troponin assays
- Coefficient of variance < 10% at 99th percentile value of reference healthy population
- Concentrations above assay's limit of detection are measurable in > 50% of healthy individuals
## PERFORMANCE HEART SCORE: 30 d MACE

<table>
<thead>
<tr>
<th>Source</th>
<th>Score</th>
<th>Class of Evidence</th>
<th>Troponin</th>
<th>Sensitivity (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Backus et al(^{47})</td>
<td>0 to 3</td>
<td>III</td>
<td>Conventional</td>
<td>98.3</td>
<td>97.2 to 100</td>
</tr>
<tr>
<td>Six et al(^{33})</td>
<td>0 to 2</td>
<td>III</td>
<td>Conventional</td>
<td>98.9</td>
<td>97.3 to 99.6</td>
</tr>
<tr>
<td>Sun et al(^{60})</td>
<td>0 to 3</td>
<td>III</td>
<td>Conventional</td>
<td>98.2</td>
<td>97.8 to 98.6</td>
</tr>
<tr>
<td>Chen et al(^{41})</td>
<td>0 to 5</td>
<td>III</td>
<td>Conventional</td>
<td>48.9</td>
<td>38.2 to 59.7</td>
</tr>
<tr>
<td>Poldevaart et al(^{56})</td>
<td>0 to 3</td>
<td>III</td>
<td>Conventional and high sensitivity</td>
<td>98.0</td>
<td>96.7 to 98.8</td>
</tr>
<tr>
<td>Van Den Berg and Body(^{57})</td>
<td>0 to 2</td>
<td>III</td>
<td>Conventional and high sensitivity</td>
<td>99.4</td>
<td>96.8 to 99.9</td>
</tr>
<tr>
<td>Carlton et al(^{40})</td>
<td>0 to 2</td>
<td>III</td>
<td>High sensitivity</td>
<td>98.7</td>
<td>92.4 to 99.9</td>
</tr>
<tr>
<td>Leung et al(^{42})</td>
<td>0 to 2 (modified)</td>
<td>III</td>
<td>High sensitivity</td>
<td>100.0</td>
<td>91.6 to 100.0</td>
</tr>
</tbody>
</table>
2. In adult patients with suspected acute NSTE ACS, can troponin testing within 3 hours of ED presentation be used to predict a low rate of 30-day MACE?

- **Level C recommendations.** In adult patients with suspected acute NSTE ACS, conventional troponin testing at 0 & 3 hours among low-risk ACS patients (defined by HEART score 0 to 3) can predict an acceptable low rate of 30-day MACE.

- **Level C recommendations.** A single high-sensitivity troponin result below the level of detection on arrival to the ED, or negative serial high-sensitivity troponin result at 0 and 2 hours is predictive of a low rate of MACE.

- **Level C recommendations.** In adult patients with suspected acute NSTE ACS who are determined to be low risk based on validated ADPs that include a nonischemic ECG result and negative serial high-sensitivity troponin testing results both at presentation and at 2 hours can predict a low rate of 30-day MACE allowing for an accelerated discharge pathway from the ED.
HEART SCORE ≤ 3 PLUS NEG TROP 0 & 3 h: Conventional Troponin

- Mahler (Circ Cardiovasc Qual Outcomes. 2015;8:195-203)
  - 282 patients randomized
  - Zero MACE missed
- MIDAS Study (Int J Cardiol. 2013;168:795-802)
  - Prospective observation cohort
  - 18 US sites
  - 1% MACE missed
CONVENTIONAL TROPONINS: 0 AND 2 HR

- Stopyra et al *Crit Pathw Cardiol. 2015;14:134-138*
  - 2 hour ADP
  - sensitivity 88.2% (95% CI 63.6% to 98.5%)
  - sensitivity 83.9% (95% CI 66.3% to 94.5%)
TIMI = 0 PLUS NEG TROP 0 & 2 h: High Sensitivity Troponin

- **ADAPT TRAIL (Class I) n=392**
  - sensitivity of 99.7% (95% CI 98.1% to 99.9%)
  - specificity of 23.4% (95% CI 21.4% to 25.4%)

- **ASPECT (Class II) n=3582**
  - sensitivity of 99.3% (95% CI 97.9% to 99.8%)
  - specificity of 11.0% (95% CI 10.0% to 12.2%)
WHAT ABOUT A SINGLE HS TROPONIN < LOD?

  - 1,138 patients
  - 1/3 with troponin < 5 ng/L (LOD)
  - Sensitivity was 99% (0.3% risk of MACE)

  - 11 studies with 2,825 patients
  - Pooled sensitivity of MACE was 98%
3. In adult patients with suspected NSTE ACS in whom acute MI has been excluded, does further diagnostic testing (eg, provocative, stress test, computed tomography [CT] angiography) for ACS prior to discharge reduce 30-day MACE?

- **Level B recommendations.** Do not routinely use further diagnostic testing (coronary CT angiography, stress testing, myocardial perfusion imaging) prior to discharge in low-risk patients in whom acute MI has been ruled out to reduce 30-day MACE.

- **Level C recommendations.** Arrange follow-up in 1 to 2 weeks for low-risk patients in whom MI has been ruled out. If no follow-up is available, consider further testing or observation prior to discharge (Consensus recommendation).
• Class II (one study)
  • Lim et al (J Nucl Cardiol. 2013;20:1002-1012) RCT on effect of stress myocardial perfusion imaging on 30-day outcomes
  • Both groups had low 30-day MACE rates: stress myocardial perfusion imaging group 0.4% vs standard management group 0.8% (RR =0.50; 95% CI 0.13 to 2.00)

• Class III (two studies)
  • Frisoli et al (Circ Cardiovasc Qual Outcomes. 2017;10: e003617) randomized 105 patients with HEART ≤ 3 and reassuring 0- and 3-h troponin I to either immediate discharge or stress testing in the ED: NO MACE
  • Poon et al (J Am Coll Cardiol. 2013;62:543-552) followed patients after coronary CT for 30-day MACE rates after NSTEMI was ruled out with ECG and serial troponins: NO MACE
4. Should adult patients with acute NSTEMI receive immediate antiplatelet therapy in addition to aspirin to reduce 30-day MACE?

- **Level C recommendations.** P2Y12 inhibitors and glycoprotein IIb/IIIa inhibitors may be given in the ED or delayed until cardiac catheterization.
Adenosine Diphosphate–Induced Platelet Aggregation Inhibitors (P2Y$_{12}$ inhibitors).

- Class I RCT (Montalescot et al: *N Engl J Med*. 2013;369:999-1010): **PRASUGREL** in patients with NSTE ACS who were to undergo catheterization
  - prasugrel before angiography did not reduce 30-day MACE
  - major bleeding episodes increased in prasugrel group at 30 days (2.8% vs 1.5%, hazard ratio 2.0; 95% CI 1.3 to 3.1)
  - reduction in MI during 12-mo study (5.2% vs 6.7%; relative risk 0.8; 95% CI 0.7 to 0.9)
  - risk of bleeding increased in clopidogrel group (8.5% vs 5.0%; relative risk 1.7; 95% CI 1.5 to 1.9)
Antiplatelet Glycoprotein IIb/IIIa Inhibitors

- **ABCIXIMAB**
  GUSTO IV-ACS Trial (Lancet. 2001;357:1915-1924)
  - no difference in 30-day death/MI (odds ratio 1.0; 95% CI 0.83 to 1.24) for placebo vs 24-hr abciximab
  - increased mortality (<1%) at 48 hr for patients receiving a 24- or 48-hr of abciximab

- **EPTIFIBATIDE or TIROFIBAN**
  ACUITY Timing Trial (JAMA 2007;297:591-602)
  - early administration (0.6 h) vs deferral until time (4.5 h) of PCI (< 72 hr) did not confer benefit
  - increased bleeding (6.1 vs 4.9% RR 1.12 [0.67-0.95])
WHAT WE DID NOT STUDY...

- Delta
- Duration of pain
- Shared decision making
CONCLUSIONS

• Patients with chest pain & low risk for ACS (e.g., HEART score ≤ 3) and normal troponin at 0 and 3 hours post presentation may be discharged safely, with ≤ 2% risk of 30-day MACE

• High-sensitivity troponins accelerate rule-out protocol (0 and 2 h)

• In low risk cases who rule out, no data to support subsequent noninvasive testing

• It is acceptable to delay further antiplatelet therapy, beyond heparin, especially if concern for bleeding